PART C

DRUGS

DIVISION I

General

C.01.001. (1) In this Part

26-9-85 "acetaminophen product" has the same meaning as in Division 9; (*produit d'acétaminophène*)

7-11-95 "adverse drug reaction" means a noxious and unintended response to a drug, which occurs at doses normally used or tested for the diagnosis, treatment or prevention of a disease or the modification of an organic function; (*réaction indésirable à une drogue*)

26-9-85 "adult standard dosage unit" has, with reference to a drug, the same meaning as in Division 9; (*dose normale pour adultes*)

"antibiotic" means any drug or combination of drugs such as those named in C.01.401 to C.01.592 which is prepared from certain micro-organisms, or which formerly was prepared from micro-organisms but is now made synthetically and which possesses inhibitory action on the growth of other micro-organisms; (*antibiotique*)

"brand name" means, with reference to a drug, the name, whether or not including the name of any manufacturer, corporation, partnership or individual, in English or French,

20-4-93 (a) that is assigned to the drug by its manufacturer,

(b) under which the drug is sold or advertised, and

(c) that is used to distinguish the drug; (*marque nominative*)

7-11-95 "case report" means a detailed record of all relevant data associated with the use of a drug in a subject; (*fiche d'observation*)

30-7-87 "child resistant package" means a package that meets the requirements of subsection (2); (*emballage protège-enfants*)

29-6-85 "children's standard dosage unit" has, with reference to a drug, the same meaning as in Division 9; *(dose normale pour enfants*)

"common name" means, with reference to a drug, the name in English or French by which the drug is

20-4-93 (a) commonly known, and

(b) designated in scientific or technical journals, other than the publications referred to in Schedule B to the Act; (*nom usuel*)

"expiration date" means the earlier of

19-11-92 (a) the date, expressed at minimum as a year and month, up to and including which a drug maintains its labelled potency, purity and physical characteristics, and

(b) the date, expressed at minimum as a year and month, after which the manufacturer recommends that the drug not be used; (*date limite d'utilisation*)

7-8-96 * "immediate container" means the receptacle that is in direct contact with a drug; (*récipient immédiat)*

"internal use" means ingestion by mouth or application for systemic effect to any part of the body in which the drug comes into contact with mucous membrane; (*usage interne*)

"official drug" means any drug

29-12-60 (i) for which a standard is provided in these Regulations, or

(ii) for which no standard is provided in these Regulations but for which a standard is provided in any of the publications mentioned in SCHEDULE B to the Act; (*drogue officielle*)

"parenteral use" means administration of a drug means of hypodermic syringe, needle or other instrument through or into the skin or mucous membrane; (*usage parentéral*)

"per cent" means per cent by weight unless otherwise stated; (*pour cent*)

25-7-63 "practitioner" means a person authorized by the law of a province of Canada to treat patients with any drug listed or described in SCHEDULE F to the Regulations; (*praticien*)

29-12-60 "prescription" means an order given by a practitioner directing that a stated amount of any drug or mixture of drugs specified therein be dispensed for the person named in the order; (*ordonnance*)

"proper name" means, with reference to a drug, the name in English or French

(i) assigned to the drug in section C.01.002,

(ii) that appears in bold-face type for the drug in these Regulations and, where the drug is dispensed in a form other than that described in this Part the name of the dispensing form,

(iii) specified in the Canadian licence in the case of drugs included in SCHEDULE C or SCHEDULE D to the Act, or

(iv) assigned in any of the publications mentioned in SCHEDULE B to the Act in the case of drugs not included in subparagraphs (i), (ii) or (iii) of this paragraph; (*nom propre*)

26-9-85 "salicylate product" has the same meaning as in Division 9; (*produit de salicylate*)

4-12-97 "serious adverse drug reaction" means a noxious and unintended response to a drug that occurs at any dose and that requires in-patient hospitalization or prolongation of existing hospitalization, causes congenital malformation, results in persistent or significant disability or incapacity, is life-threatening or results in death; (*réaction indésirable grave à une drogue*)

7-11-95 "serious unexpected adverse drug reaction" means a serious adverse drug reaction that is not identified in nature, severity or frequency in the risk information set out on the label of the drug; (*réaction indésirable grave et imprévue à une drogue*)

"teaspoon" means, for the purpose of calculation of dosage, a volume of five cubic centimetres. (*cuillerée à thé*)

30-7-87 "test group" means a group that meets the requirements of subsection (3). (*groupe d'essai*)

16-8-95 "withdrawal period" means the length of time between the last administration of a drug to an animal and the time when tissues or products collected from the treated animal for consumption as food contain a level of residue of the drug that would not likely cause injury to human health. (*délai d'attente*)

(2) A child resistant package is a package that

(a) when tested in accordance with an acceptable method,
- (i) in the case of a test group comprising children, cannot be opened
  - (A) by at least 85 per cent of those children prior to a demonstration to them of the proper means of opening the package, and
  - (B) by at least 80 per cent of those children after the demonstration, and
- (ii) in the case of a test group comprising adults
  - (A) can be opened by at least 90 per cent of those adults, and

30-7-87
  - (B) where the package is designed so that, once opened and reclosed, it continues to meet the requirements of subparagraph (i), can be so reclosed by at least 90 per cent of those adults; or

30-4-96 (b) complies with the requirements of one of the following standards, namely,

1-7-97
- (i) Canadian Standards Association Standard CAN/CSA-Z76.1-M90, entitled *Recloseable Child-Resistant Packages*, published January 1990, as amended from time to time,
- (ii) European Standard EN 28317:1992, entitled *Child-resistant packaging – Requirements and testing procedures for reclosable packages* , as adopted by the European Committee for Standardization on October 30, 1992, recognized by the British Standards Institution, and effective February 15, 1993 and by the Association française de normalisation, and effective December 20, 1992, and which reiterates fully the international standard ISO 8317:1989, as amended from time to time, and
- (iii) *Code of Federal Regulations* (United States), Title 16, Section 1700.15, entitled *Poison prevention packaging standards*, as amended from time to time.

(3) For the purposes of this section, "test group" means

(a) in relation to children, a group of at least 200 children who
- (i) are healthy and have no obvious physical or mental disability,
- (ii) are between 42 and 51 months of age, and
- (iii) represent evenly, within plus or minus 10 per cent, each monthly age between 42 and 51 months calculated to the nearest month; and

30-7-87 (b) in relation to adults, a group of at least 100 adults who
- (i) are healthy and have no obvious physical or mental disability,
- (ii) are between 18 and 45 years of age, and
- (iii) represent evenly, within plus or minus 10 per cent, each yearly age between 18 and 45 years calculated to the nearest year.

30-4-96 * (4) For the purpose of this section, an amendment from time to time to a standard referred to in paragraph (2)(b) becomes effective 18 months after the date designated by the competent authority as the effective date for the amendment.

26-8-98 **C.01.001A.** Repealed by P.C. 1998-1461 of August 26, 1998.

C.01.002. The Proper Name of a drug shown opposite an item number in the following Table is the column headed "Chemical Names and Synonyms" shall be the name shown opposite that item number in the column headed "Proper Names":

TABLE

Item No.	Proper Names	Chemical Names and Synonyms
A.1	Acepromazine	2-acetyl-10-(3-dimethylaminopropyl) phenothiazine
A.2	Acetaminophen	**p**-Acetaminophenol, Paracetamol, **p**-Hydroxyacetanilide: N-acetyl- **p**-aminophenol
A.3	Acetanilide: Acetanilid	Acetylaminobenzene: Antifebrin: Phenylacetamide
A.4	Acetylsalicylic acid	Acetylsalicylic acid
A.5	Allopurinol	1-H-Pyrazolo[3,4-**d**]pyrimidin-4-ol: 4-Hydroxypyrazolo(3,4-**d**)pyrimidine
A.6	Amantadine	1-Adamantanamine
A.7	Aminocaproic, acid	6-Aminohexanoic acid
A.8	Aminopterin	N-[4-(2,4-diamino-6-pteridyl methyl) amino-benzoyl]-L-glutamic acid
A.9	Aminopyrine: Amidopyrine	1,5-dimethyl-2-phenyl-4-dimethylamino-3-pyrazolone: Dimethylaminophenazone
A.10	Amitriptyline	3-(3-Dimethylaminopropylidene)-1,2: 4,5-dibenzocyclohepta-1,4-diene
A.11	Azacyclonol	α,α-diphenyl-4-piperidinecarbinol
B.1	Bemegride	3-Ethyl-3-methylglutarimide
B.2	Benactyzine	Dimethylaminoethyl-1,1-diphenylglycolate
B.3	Bendroflumethiazide	3-benzyl-3,4-dihydro-6-(trifluoromethyl)-2H-1,2,4-benzothiadiazine-7-sulfonamide-1,1-dioxide: Bendrofluazide (B.A.N.)
B.4	Betahistine	2-[2-(Methylamino)ethyl] pyridine
B.5	Bethanidine	N-Benzyl-N'N"-dimethylguanidine: 1-Benzyl-2,3-dimethylguanidine
B.6	Bretylium tosylate	N-2-Bromobenzyl-N-ethyl-N,N-dimethylammonium tosylate (Tosylic acid is trivial name for **p**-toluenesulphonic acid)
B.7	Bromisoval	2-monobromoisovalerylurea: Bromisovalum: Bromvalitone
C.1	Calcium Carbimide	Calcium cyanamide
C.2	Captodiamine	4-butylthio-α-phenylbenzyl-2-dimethylaminoethylsulfide
C.3	Carisoprodol	N-Isopropyl-2-methyl-2-propyl-1,3-propanediol dicarbamate
C.4	Carphenazine	1-{10-(3[4-(2-Hydroxyethyl)-1-piperazinyl] propyl)-phenothiazin-2yl}-1-propapone
C.5	Cephaloridine	7-[(2-Thienyl) acetamido]-3-(1-pyridylmethyl)-3-cephem-4-carboxylic acid betaine
C.6	Chlormezanone	2-(4-chlorophenyl)-3-methyl-4-methathiazanone-1,1-dioxide: Chlormethazone: Chlormethazanone
C.7	Chloromethapyrilene	N,N-dimethyl-N'-(2-pyridly)-N'-(5-chloro-2-thenyl)-ethylenediamine: Chlorothen
C.8	Chlorphentermine	4-Chloro-α,α-dimethylphenethylamine
C.9	Cinchocaine	2-butoxy-N-(2-diethylaminoethyl) cinchoninamide: Dibucaine
C.10	Cinchophen	2-phenylquinoline-4-carboxylic acid: Quinophan
C.11	Clofibrate	Ethyl 2-(**p**-chlorophenoxy)-2-methylpropionate

TABLE -- Continued

	Item No.	Proper Names	Chemical Names and Synonyms
	C.12	Clomiphene	1-Chloro-2-[4-(2-diathylaminoethoxy) phenyl]-1,2-diphenylethylene: 2-[**p**-(2-Chloro-1,2-diphenylvinyl)phenoxy] triethylamine
	D.1	Desipramine	5-(3-Methylaminopropyl)-10,11-dihydro-5H-dibenz[b,f]azepine
	D.2	Diazepam	7-Chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one
	D.3	Diethylpropion	1-phenyl-2-diethylaminopropanone-1
	D.4	Diphenidol	1,1-Diphenyl-4-piperidinobutan-1-ol
	D.5	Disulfiram	Tetraethylthiuram disulphide
	E.1	Ectylurea	2-ethyl-*cis*-crotonylurea
	E.2	Emylcamate	1-Ethyl-1-methylpropyl carbamate
	E.3	Ethacrynic Acid	[2,3-Dichloro-4-(2-methylenebutyryl) phenoxyl] acetic acid: 2,3-Dichloro-4-(2-ethylacryloyl) phenoxyacetic acid
	E.4	Ethchlorvynol	3-(2-chlorovinyl)-1-pentyn-3-ol
	E.5	Ethinamate	1-ethynylcyclohexyl carbamate
	E.6	Ethionamide	2-Ethylisonicotinthioamide
	E.7	Ethomoxane	2-**n**-Butylaminomethyl-8-ethoxybenzo-1,4-dioxan
	E.8	Ethyl Trichloramate	Ethyl **n**-[1-(2,2,2-trichloro-1-hydroxy-ethyl)] carbamate
	E.9	Etryptamine	3-(2-Aminobutyl) indole
	E.10	Etymemazine	10-(3-Dimethylamino-2-methylpropyl)-2-ethylphenothiazine
	F.1	Fluphenazine	10-{3-[4-(2-Hydroxyethyl)piperazine-1-yl] propyl}-2-trifluoromethylphenothiazine
	F.2	Furosemide	4-Chloro-N-furfuryl-5-sulphamoylanthranilic acid: Frusemide (B.A.N.)
17-9-87	G.1	Glyburide	5-chloro-N-[2-[4-[[[(cyclohexylamino carbonyl]amino]sulfonyl]phenyl]ethyl]-2-methoxy benzamide: 1-4[4-[2-(5-chloro-2-methoxybenzamido)ethyl]phenylsulfonyl]-3-cyclohexylurea: Glibenclamide
	H.1	Haloperidol	4-(4-Chlorophenyl)-1-[3-(4-fluorobenzoyl) propyl]-piperidin-4-ol: 4-[4- **p**-Chloro-phenyl)-4-hydroxypiperidino]-4'-fluoro-butyrophenone
	H.2	Hydroxychloroquine	7-Chloro-4[4-(N-ethyl-N-2-hydroxyethyl-amino)-1-methylbutyl-amino] quinoline
	H.3	Hydroxyzine	1-(**p**-chloro-α-phenylbenzyl)-4-(2-hydroxy ethoxyethyl)piperazine
	I.1	Idoxuridine	5-Iodo-2'-deoxyuridine
	I.2	Imipramine	5-(3-dimethylaminopropyl)-10,11-dihydro-5H-dibenz[b,f]azepine
	I.3	Indomethacin	1-(**p**-Chlorobenzoyl)-5-methoxy-2-methyl-indole-3-acetic acid
	I.4	Iproniazid	1-isonicotinoyl-2-isopropylhydrazine
	I.5	Isocarboxazid	3-N-Benzylhydrazinocarbonyl-5-methyl-isoxazole
	I.6	Isoproterenol	3,4-Dihydroxy-α-[(isopropylamino) methyl] benzyl alcohol: Isoprenaline
	L.1	Liothyronine	L-α-Amino-3-[(4-hydroxy-3-iodophenoxy) -3,5-di-iodo-phenyl] propionic acid

TABLE -- Continued

Item No.	Proper Names	Chemical Names and Synonyms
M.1	Mefenamic acid	N-(2,3-Xylyl)-anthranilic acid
M.2	Melphalan	4-Di-(2-chloroethyl)amino-L-phenylalanine
M.3	Mepazine	10-[(1-methyl-3-piperidyl) methyl] phenothiazine
M.4	Mephenesin	3-**o**-toloxy-1,2-propanediol
M.5	Mephenoxalone	5-(**o**-Methoxyphenoxymethyl)-2-oxazolidinone
M.6	Meprobamate	2,2-di(carbamoylmethyl) pentane
M.7	Methaqualone	2-Methyl-3-**o**-tolyquinazolin-4-one: 2-Methyl-3-**o**-tolyl-4-quinazolone
M.8	Methisazone	1-Methylindoline-2,3-dione-3-thiosemicarbazone: N-Methylisatin-β-thiosemicarbazone
M.9	Methotrimeprazine	10-[3-(2-Methyl)dimethylamino propyl]-2-methoxyphenothiazine: Levomepromazine
M.10	Methyldopa	1-3-(3,4-Dihydroxyphenyl)-2-methylalanine
M.11	Methylparafynol	3-methyl-1-pentyn-3-ol: Methylpentynol
M.12	Methylphenidate	Methyl-1-phenyl-1-(2-piperidyl) acetate
M.13	Methyprylon	3,3-diethyl-5-methyl-2,4-piperidinedione
M.14	Methysergide	1-(Hydroxymethyl)propylamide of 1-methyl-*d*-lysergic acid
M.15	Metyrapone	2-Methyl-1,2-di(3-pyridyl)propan-1-one
N.1	Nalidixic Acid	1-Ethyl-7-methyl-4-oxo-1,8-naphthyridine-3-carboxylic acid
N.2	Nialamide	1-[2-(benzycarbamyl)ethyl]-2-isonicotinoylhydrazine
N.3	Nortriptyline	3-(3-Methylaminopropylidene)-1,2,4,5-dibenzocyclohepta-1,4-diene
O.1	Oxanimide	2-ethyl-3-propyl-glycidamide
O.2	Oxazepam	7-Chloro-1,3-dihydro-3-hydroxy-5-phenyl-1,4-benzodiazepin-2-one
O.3	Oxyphenbutazone	4-**n**-Butyl-2-(4-hydroxyphenyl)-1-phenyl-pyrazolidine-3,5-dione
P.1	Paramethadione	3,5-dimethyl-5-ethyl-2,4-oxazolidinedione
P.2	Pargyline	N-Benzyl-N-methylprop-2-ynylamine
P.3	Pemoline	2-Imino-5-phenyloxazolidin-4-one
P.4	Pentazocine	1,2,3,4,5,6-Hexahydro-8-hydroxy-6,11-dimethyl-3-(3-methylbut-2-enyl)-2,6-methano-3-benzazocine: 1,2,3,4,5,6-Hexahydro-6,11-dimethyl-3-(3-methyl-2-butenyl)-2,6-methano-3-benzazocin-8-ol
P.5	Pentolinium Tartrate	NN'-Pentamethylenedi-(methylpyrrolidinium hydrogen tartrate)
P.6	Perphenazine	2-chloro-10-{3-[1-(2-hydroxyethyl)-4-piperazinyl]propyl} phenothiazine
P.7	Phacetoperane	*l*-1-Phenyl-1-(2'-piperidyl)-1-acetoxy-methane
P.8	Phenacemide	(Phenylacetyl)urea
P.9	Phenacetin	**p**-acetphenetidin: Acetphenetidin: Acetophenetidin: **p**-ethoxyacetanilid
P.10	Phenaglycodol	2-**p**-chlorophenyl-3-methyl-2,3-butanediol
P.11	Phendimetrazine	3,4-Dimethyl-2 Phenylmorpholine
P.12	Phenelzine	2-phenylethylhydrazine
P.13	Phenformin	N'-β-phenethylformamidinyliminourea
P.14	Pheniprazine	α-Methylphenethylhydrazine
P.15	Phenmetrazine	Tetrahydro-3-methyl-2-phenyl-1,4-oxazine: 3-methyl-2-phenylmorpholine
P.16	Phentermine	α,α-Dimethylphenethylamine: phenyl-tert-butylamine
P.17	Phenylindanedione	2-phenylindane-1,3-dione

TABLE -- Continued

	Item No.	Proper Names	Chemical Names and Synonyms
	P.18	Phenyltoloxamine	N,N-dimethyl-2-(a-phenyl-o-tolyloxy) ethylamine
	P.19	Pholedrine	**p**-(4-hydroxyphenyl)-isopropylmethylamine
	P.20	Piperliate	1-piperidine-ethanol benzilate
	P.21	Pipradrol	Diphenyl-2-piperidylmethanol
	P.22	Prochlorperazine	2-Chloro-10-[3-(1-methyl-4-piperazinyl) propyl] phenothiazine
	P.23	Prodilidine	1,2-Dimethyl-3-phenyl-3-pyrrolidinyl propionate
	P.24	Propranolol	1-(Isopropylamino)-3-(1-naphthyloxy)-2-propanol
	P.25	Prothipendyl	9-(3-Dimethylaminopropyl)-10-thia-1,9-diaza-anthracene
	P.26	Protriptyline	7-(3-Methylaminopropyl)-1,2:5,6-dibenzo-cycloheptatrien: N-Methyl-5H-dibenzo [a,d] cycloheptene-5-propylamine
	P.27	Pyrazinamide	Pyrazinoic acid amide
	R.1	Rifampin	3-{[(4-methyl-1-piperazinyl)imino]methyl} rifamycin SV: Rifampicin (I.N.N.) (Rifamycin SV is an antibiotic produced by Streptomyces mediterranci)
17-3-88	S.01	Sodium Cromoglycate	4H-1-Benzopyran-2-carboxylic acid,5,5'-[(2-hydroxy-1,3-propanediyl) bis(oxy)] bis [4-oxo,disodium salt]: Disodium 5,5'-(2-hydroxytrimethylenedioxy) bis[4-oxo-4H-1-benzopyran-2-carboxylate]: Disodium 4,4'-dioxo-5,5'-(2-hydroxytrimethylene-dioxy)di (chromene-2-carboxylate): Cromolyn Sodium (USP): Disodium Cromoglycate
	S.1	Sulfameter	2-(4-Aminobenzenesulphonamido)-5-methoxy-pyrimidine: N'-(5-methoxy-2-pyrimidinyl) sulfanilamide: Sulfamethoxydiazine (B.A.N.)
	S.2	Sulfamethazine	N'-(4,6-dimethyl-2-pyrimidyl)sulfanilamide: 2-(**p**-aminobenzenesuylphonamide)-4,6-dimethylpyrimidine: sulphadimedine
	S.3	Sulfinpyrazone	1,2-diphenyl-4-(2-phenylsulfinilethyl)-3,5-pyrazolidinedione
	S.4	Sulfisoxazole	3,4-dimethyl-5-sulfanilamidoisoxazole: Sulphafurazole
	T.1	Tetracaine	2-dimethylaminoethyl-**p**-**n**-butylamino-benzoate: Amethocaine
	T.2	Thiethylperazine	2-Ethylthio-10-[3-(4-methylpiperazin-1-yl) propyl]phenothiazine
	T.3	Thiopropazate	2-chloro-10-{3-[1-(2-acetoxyethyl)-4-piperazinyl]propyl}phenothiazine
	T.4	Thioproperazine	2-Dimethylsulphamoyl-10-[3-(4-methyl-piperazin-1-yl)propyl]phenothiazine
	T.5	Thioridazine	10-{2-[2-(1-methylpiperidyl)] ethyl}-2-methylthiophenothiazine
	T.6	Tranylcypromine	Trans d, 1-2-phenylcyclopropylamine
	T.7	Triamterene	2,4,7-Triamino-6-phenylpteridine
	T.8	Triflupromazine	10-(3-dimethylaminopropyl)-2-trifluoro-methylphenothiazine: Fluopremazine
	T.9	Trimeprazine	10-(3-dimethylamino-2-methylpropyl) phenothiazine
	T.10	Trimethadione	3,5,5-trimethyl-2,4-oxazolidinedione: Troxidone

TABLE -- Concluded

Item No.	Proper Names	Chemical Names and Synonyms
T.11	Trimipramine	5-(3-Dimethylamino-2-methylpropyl)-10,11-dihydro-5H-dibenz[b,f]azepine: 5-(3'-Dimethylamino-2'-methylpropyl)iminodibenzyl
T.12	Tybamate	2-Methyl-2-propyltrimethylene butylcarbamate carbamate: 2-(Hydroxymethyl)-2-methylpentyl butylcarbamate carbamate
V.1	Vinblastine	An alkaloid derived from *Vinca rosea*
V.2	Vincristine	An alkaloid derived from *Vinca rosea*

10-7-80 **C.01.003.** No person shall sell a drug that is not labelled as required by these Regulations.

C.01.004. (1) The inner and outer labels of a drug shall show

17-5-01 (a) on the principal display panel

20-4-93 (i) the proper name, if any, of the drug which, if there is a brand name for the drug, shall immediately precede or follow the brand name in type not less than one-half the size of that of the brand name,

(ii) if there is no proper name, the common name of the drug,

(iii) where a standard for the drug is prescribed in Division 6 of this Part, a statement that the drug is a Canadian Standard Drug, for which the abbreviation C.S.D. may be used,

28-8-90 (iv) where a standard for the drug is not prescribed in Division 6 of this Part but is contained in a publication mentioned in Schedule B to the Act, the name of the publication containing the standard used or its abbreviation as provided in Schedule B or, if a manufacturer's standard is used, a statement setting forth the fact that such a standard is used, and

(v) in both official languages, the notation "sterile" " *stérile*" if the drug is required to be sterile by these Regulations;

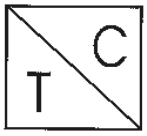
17-5-01 (b) on the upper left quarter of the principal display panel

10-7-80 (i) the symbol " **Pr** " in the case of a drug required by this Part or Part D to be sold on prescription, but in no other case shall the symbol " **Pr** " appear on the label of a drug,

20-11-97 (ii) the symbol "  " in a clear manner and a conspicuous colour and size, in the case of a controlled drug, other than a controlled drug contained in an agricultural implant and set out in Part III of the schedule to Part G, and

14-5-97 (iii) the symbol " **N** " in a colour contrasting with the rest of the label or in type not less than half the size of any letters used thereon, in the case of a narcotic as defined in the *Narcotic Control Regulations*; and

1-6-00 (iv) in the case of a targeted substance as defined in subsection 1(1) of the *Benzodiazepines and Other Targeted Substances Regulations*, the following symbol in a colour contrasting with the rest of the label and in type not less than half the size of any other letter used on the main panel, namely,



(c) on any panel

(i) the name and address of the manufacturer of the drug,

10-7-80 (ii) the lot number of the drug,

(iii) adequate directions for use of the drug,

(iv) a quantitative list of the medicinal ingredients of the drug by their proper names or, if they have no proper names, by their common names, and

19-11-92 (v) the expiration date of the drug.

(2) In addition to the requirements of subsection (1), the outer label of a drug shall show

(a) the net amount of the drug in the container in terms of weight, measure or number;

(b) in the case of a drug intended for parenteral use, a quantitative list of any preservatives present therein by their proper names or, if they have no proper names, by their common names; and

28-4-89 (c) in the case of a drug for human use that contains mercury or a salt or derivative thereof as a preservative, a quantitative list of all mercurial preservatives present therein by their proper names or, if they have no proper names, by their common names.

5-4-90 (3) Where the container of a drug is too small to accommodate an inner label that conforms to the requirements of these Regulations, the inner label requirements of these Regulations do not apply to the drug in that container if

(a) there is an outer label that complies with the labelling requirements of these Regulations; and
(b) the inner label shows
20-4-93 (i) the proper name of the drug, the common name of the drug if there is no proper name or, in the case of a drug with more than one medicinal ingredient, the brand name of the drug,
23-4-81 (ii) the potency of the drug except where, in the case of a drug with more than one medicinal ingredient, the name used pursuant to subparagraph (i) for that drug is unique for a particular potency of the drug,
(iii) the net contents of the drug if it is not in a discrete dosage form,
(iv) the route of administration of the drug if other than oral,
(v) the lot number of the drug,
(vi) the name of the manufacturer of the drug,
19-11-92 (vii) the expiration date of the drug, and
(viii) the identification of special characteristics of the dosage form if they are not evident from the name of the drug under subparagraphs (i) or (ii).

19-11-92 (4) Revoked by P.C. 1992-2327 of November 19, 1992.

(5) This section does not apply to

(a) a drug sold to a drug manufacturer; or
(b) a drug dispensed pursuant to a prescription, if its label carries suitable directions for use and complies with the requirements of section C.01.005.

C.01.004.1 (1) No person shall import a drug in dosage form into Canada for the purpose of sale unless they have in Canada a person who is responsible for the sale of the drug.
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(2) No person who imports a drug in dosage form into Canada shall sell any lot or batch of the drug unless the name of the person who imports it, and the address of the principal place of business in Canada of the person responsible for its sale, appears on the inner and outer labels of the drug.

17-5-01 **C.01.005.** (1) The principal display panel of both the inner label and outer label of a drug sold in dosage form shall show in a clear and legible manner the drug identification number assigned by the Director for that drug pursuant to subsection C.01.014.2(1), preceded by the words "Drug Identification Number" or "Drogue : identification numérique" or both, or the letters "DIN".

26-8-98 *Note:* A manufacturer may, until September 30, 2000, label a drug with the label that was in use on September 30, 1998.

24-4-75 (a) where the drug is not a proprietary medicine as defined in subsection C.10.001 (1), by the word "Drug Identification Number" or "drogue: identification numérique" or both, or their abbreviation "DIN"; or
3-2-76 (b) where the drug is a proprietary medicine as defined by subsection C.10.001(1), by the letters "GP"

(2) Subsection (1) does not apply to a drug

(a) compounded by a pharmacist pursuant to a prescription or by a practitioner; or
4-10-73 (b) sold pursuant to a prescription, where the label of that drug indicates:
20-4-93 (i) the proper name, the common name or the brand name of the drug,
(ii) the potency of the drug; and
(iii) the name of the manufacturer of the drug.

19-3-81 (3) For the purposes of this section and section C.01.014, "a drug in dosage form" means a drug in a form in which it is ready for use by the consumer without requiring any further manufacturing.

C.01.006. Where a package of a drug has only one label, that label shall contain all the information required by these regulations to be shown on both the inner and the outer labels.

C.01.007. No reference, direct or indirect, to the Act or to these regulations shall be made upon any label of or in any advertisement for a drug unless such reference is a specific requirement of the Act or these regulations.

C.01.008. Revoked by P.C. 1980-1850 of July 10, 1980.

C.01.009. Where by any statute of the Parliament of Canada or any regulation made thereunder a standard or grade is prescribed for a drug and that standard is given a name or designation by such statute or regulation, no person shall on a label of or in any advertisement for that drug use that name or designation unless the drug conforms with the standard or grade.

15-6-67 **C.01.010.** Where it is necessary to provide adequate directions for the safe use of a parenteral drug or SCHEDULE F drug that is used in the treatment or prevention of any disease, disorder or abnormal physical state mentioned in SCHEDULE A to the Act, such diseases, disorders or abnormal physical states may be mentioned on the labels and inserts accompanying that drug and to such extent, that drug is hereby exempted from the provisions of section 3 of the Act.

19-11-68 **C.01.011.** (1) A drug referred to in subsection (2) of section 10 of the Act shall be exempt from the standard for any drug contained in any publication mentioned in Schedule B to the Act to the extent that such drug differs from that standard with respect to colour, flavour, shape and size, if such difference does not interfere with any method of assay prescribed in any such publication.

11-5-93 (2) Revoked by P.C. 1993-940 of May 11, 1993.

(3) Where a manufacturer's standard is used for a drug, the manufacturer shall make available to the Director, on request, details of that standard and of method of analysis for the drug acceptable to the Director.

19-11-68 (4) No person shall use a manufacturer's standard for a drug that provides

(a) a lesser degree of purity than the highest degree of purity;
(b) a greater variation in potency than the least variation in potency,

provided for that drug in any publication mentioned in Schedule B to the Act.

C.01.012. A manufacturer who makes representations on a label of a drug in oral dosage form, or in any advertisement, with respect to the site, rate or extent of release to the body of a medicinal ingredient of the drug, or the availability to the body of a medicinal ingredient of the drug, shall

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(a) before making the representations, conduct such investigations, using an acceptable method, as may be necessary to demonstrate that the site, rate or extent of release to the body of the medicinal ingredient of the drug and the availability to the body of the medicinal ingredient of the drug, correspond to the representations; and

28-2-64 (b) on request submit the record of such investigations to the Director.

C.01.013. (1) Where the manufacturer of a drug is requested in writing by the Director to submit on or before a specified day evidence with respect to a drug, the manufacturer shall make no further sales of that drug after that day unless he has submitted the evidence requested.

(2) Where the Director is of the opinion that the evidence submitted by a manufacturer, pursuant to subsection (1), is not sufficient, he shall notify the manufacturer in writing that the evidence is not sufficient.

23-6-71 (3) Where, pursuant to subsection (2), a manufacturer is notified that the evidence with respect to a drug is not sufficient, he shall make no further sales of that drug unless he submits further evidence and is notified in writing by the Director that further evidence is sufficient.

(4) A reference in this section to evidence with respect to a drug means evidence to establish the safety of the drug under the conditions of use recommended and the effectiveness of the drug for the purposes recommended.

Assignment and Cancellation of Drug Identification Numbers

C.01.014. (1) No manufacturer shall sell a drug in dosage form unless a drug identification number has been assigned for that drug and the assignment of the number has not been cancelled pursuant to section C.01.014.6.

19-12-96 (2) Subsection (1) does not apply in respect of a drug listed in Schedule C to the Act, whole blood and its components, or a medicated feed as defined in section 2 of the *Feeds Regulations, 1983*.

C.01.014.1 (1) A manufacturer of a drug, a person authorized by a manufacturer or, in the case of a drug to be imported into Canada, the importer of the drug may make an application for a drug identification number for that drug

19-3-81 (2) An application under subsection (1) shall be made to the Director in writing and shall set out the following information:

(a) the name of the manufacturer of the drug as it will appear on the label;
(b) the pharmaceutical form in which the drug is to be sold;
(c) in the case of any drug other than a drug described in paragraph (d), the recommended route of administration;
(d) in the case of a drug for disinfection in premises, the types of premises for which its use is recommended;
(e) a quantitative list of the medicinal ingredients contained in the drug by their proper names or, if they have no proper names, by their common names;
20-4-93 (f) the brand name under which the drug is to be sold;
(g) whether the drug is for human use, veterinary use or disinfection in premises;
(h) the name and quantity of each colouring ingredient that is not a medicinal ingredient;
(i) the use or purpose for which the drug is recommended;
(j) the recommended dosage of the drug;
19-3-81 (k) the address of the manufacturer referred to in paragraph (a) and, where the address is outside the country, the name and address of the importer of the drug;
(l) the name and address of any individual, firm, partnership, or corporation, other than the names and addresses referred to in paragraphs (a) and (k), that will appear on the label of the drug;
(m) the written text of all labels and package inserts to be used in connection with the drug and of any further prescribing information stated to be available on request; and
(n) the name and position of the person who signed the application and the date of signature.

26-8-98 (3) In the case of a new drug, a new drug submission or an abbreviated new drug submission filed pursuant to section C.08.002 or C.08.002.1 shall be regarded as an application for a drug identification number.

C.01.014.2 (1) Subject to subsection (2), if a manufacturer or importer has provided all the information described in subsection C.01.014.1(2) or section C.08.002 or C.08.002.1, as the case may be, in respect of a drug, the Director shall issue to the manufacturer or importer a document that

26-8-98 (a) sets out

(i) the drug identification number assigned for the drug, preceded by the letters "DIN", or

(ii) if there are two or more brand names for the drug, the drug identification numbers assigned by the Director for the drug, each of which pertains to one of the brand names and is preceded by the letters "DIN"; and

(b) contains the information referred to in paragraphs C.01.014.1(2)(a) to (f).

(2) Where the Director believes on reasonable grounds that a product in respect of which an application referred to in section C.01.014.1 has been made

(a) is not a drug, or

(b) is a drug but that its sale would cause injury to the health of the consumer or purchaser or would be a violation of the Act or these Regulations,

he may refuse to issue the document referred to in subsection (1).

(3) Where the Director, pursuant to subsection (2), refuses to issue the document, the applicant may submit additional information and request the Director to reconsider his decision.

19-3-81 (4) On the basis of the additional information submitted pursuant to subsection (3), the Director shall reconsider the grounds on which the refusal to issue the document was made.

26-8-98 **C.01.014.3** The manufacturer or importer or person authorized by the manufacturer or importer shall, within 30 days after commencing sale of a drug, date and sign the document issued pursuant to subsection C.01.014.2(1) in respect of the drug and return the document

(a) with a confirmation that the information recorded therein is correct;

(b) indicating the date on which the drug was first sold in Canada; and

(c) accompanied by samples or facsimiles of all labels and package inserts and any further prescribing information stated to be available on request.

26-8-98 **C.01.014.4** If the information referred to in subsection C.01.014.1(2) in respect of a drug is no longer correct owing to a change in the subject matter of the information,

30-4-92 (a) in the case of a change in the subject matter of any of the information referred to in paragraphs C.01.014.1(2)(a) to (f)

(i) that occurs prior to the sale of the drug, a new application shall be made, or

(ii) that occurs after the sale of the drug, no further sale of the drug shall be made until a new application for a drug identification number in respect of that drug is made and a number is assigned; and

30-4-92 (b) in the case of a change in the subject matter of any of the information referred to in paragraphs C.01.014.1(2)(g) to (k)

(i) that occurs prior to the sale of the drug, the particulars of the change shall be submitted with the return of the document referred to in section C.01.014.3, or

(ii) that occurs after the sale of the drug, the person to whom the drug identification number in respect of that drug was issued shall, within 30 days of the change, inform the Director of the change.

C.01.014.5 Every manufacturer of a drug shall, annually before the first day of October and in a form authorized by the Director, furnish the Director with a notification signed by the manufacturer or by a person authorized to sign on his behalf, confirming that all the information previously supplied by the manufacturer with respect to that drug is correct.

C.01.014.6 (1) The Director shall cancel the assignment of a drug identification number for a drug where

(a) the person to whom the number was assigned advises that the sale or import of the drug has been discontinued;

(b) the drug is a new drug in respect of which the notice of compliance has been suspended pursuant to section C.08.006; or

(c) it has been determined that the product in respect of which the number was assigned is not a drug.

(2) The Director may cancel the assignment of a drug identification number for a drug where

(a) the manufacturer of the drug has failed to comply with section C.01.014.5; or

19-3-81 (b) the manufacturer to whom the number was assigned has been notified pursuant to section C.01.013 that the evidence he submitted in respect of the drug is insufficient.

C.01.014.7 Where a person who has been assigned a drug identification number for a drug discontinues sale of the drug in Canada, he shall, within 30 days of such discontinuation, inform the Director that he is no longer selling the drug.

Tablet Disintegration Times

C.01.015. (1) Subject to subsection (2), no person shall sell for human use a drug in the form of a tablet that is intended to be swallowed whole unless, when tested by the official method DO-25, Determination of the Disintegration Time of Tablets, dated July 5, 1989,

(a) in the case of an uncoated tablet, the tablet disintegrates in not more than 45 minutes;

(b) in the case of a plain coated tablet, the tablet disintegrates in not more than 60 minutes; and

(c) in the case where the label of the drug indicates that the tablet carries an enteric coating or a coating designed to serve a purpose similar to that of an enteric coating, the tablet does not disintegrate when exposed for 60 minutes to simulated gastric fluid, but when it is subsequently exposed for a continuous period to simulated intestinal fluid the tablet disintegrates in not more than 60 minutes.

(2) Subsection (1) does not apply in respect of a drug in the form of a tablet where

21-9-89 (a) a notice of compliance in respect of the drug in the form of a tablet has been issued pursuant to section C.08.004;

26-8-98 (b) Repealed by P.C. 1998-1461 of August 26, 1998.

21-9-89 (c) a dissolution or disintegration test for the drug in the form of a tablet is prescribed in Division 6 of this Part;

(d) the drug is labelled as complying with a standard contained in a publication referred to in Schedule B to the Act;

(e) the drug has been demonstrated by an acceptable method to be available to the body; or

13-1-94 (f) representations regarding the drug are made on its label, or in any advertisement, with respect to the site, rate or extent of release to the body of a medicinal ingredient of that drug, or the availability to the body of a medicinal ingredient of that drug.

Adverse Drug Reaction Reporting

C.01.016. (1) No manufacturer shall sell a drug unless the manufacturer, with respect to any adverse drug reaction or any serious adverse drug reaction known to the manufacturer that occurs after this section comes into force, furnishes to the Director

(a) a report of all information in respect of any serious adverse drug reaction that has occurred in Canada with respect to the drug, within 15 days after receiving the information; and

(b) a report of all information in respect of any serious unexpected adverse drug reaction that has occurred outside Canada with respect to the drug, within 15 days after receiving the information.

(2) The manufacturer shall, on an annual basis and whenever requested to do so by the Director, conduct a concise, critical analysis of the adverse drug reactions and serious adverse drug reactions to a drug referred to in subsection (1) and prepare a summary report in respect of the reports received during the previous twelve months or received during such period of time as the Director may specify.

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(3) Where, after reviewing any report furnished pursuant to subsection (1) and any available safety data relating to the drug, the Director considers that the drug may not be safe when used under the recommended conditions of use, the Director may, for the purpose of assessing the safety of the drug, request in writing, that the manufacturer submit

(a) case reports of all adverse drug reactions and serious adverse drug reactions to that drug that are known to the manufacturer; and

(b) a summary report prepared pursuant to subsection (2).

(4) The manufacturer shall submit the case reports and summary report referred to in subsection (3) within 30 days after receiving the request from the Director.

7-11-95 **C.01.017.** The manufacturer shall maintain records of the reports and case reports referred to in section C.01.016 for auditing purposes.

Limits of Drug Dosage

2-2-84 **C.01.021.** Except as provided in these Regulations, no person shall sell a drug for human use listed in the following table unless both the inner and outer labels other than the inner label of a single dose container carry a statement of

(a) the quantitative content of the drug, and
(b) the recommended single and daily adult dose designated as such, except for
  (i) preparations solely for external use, or
  (ii) preparations solely for children's use, and
(c) adequate directions for use when the drug is recommended for children which shall be either
  (i) the statement, "CHILDREN: As directed by the physician", or
  (ii) a suitably reduced maximum single and daily dose which shall not exceed the following:

Age in years	*Proportion of adult dose*
10-14	one-half
5-9	one-fourth
2-4	one-sixth
under 2 years	as directed by physician.

TABLE OF LIMITS OF DRUG DOSAGE FOR ADULTS

	Item	*External Use* --- *Maximum Limit*	*Internal Use* --- *Maximum Dosage* *Unless otherwise stated, doses are in milligrams*	
		Per cent	*Single*	*Daily*
14-1-88	Acetaminophen	--	650.0	4.0g
2-1-58	Acetanilide and derivatives (except N-Acetyl- **p**-aminophenol)	--	65.0	195.0
2-2-84	Acetylsalicylic acid	--	650.0	4.0g
	Revoked by P.C. 1984-337 of February 2, 1984			
	Aconitine, its preparations and derivatives	0.02	0.1	0.1
	Adonis vernalis	--	65.0	195.0
	Amylocaine, its salts and derivates when sold or recommended for ophthalmic use	0.0	0.0	0.0
24-7-85	Amylocaine Hydrochloride, except when sold or recommended for ophthalmic use	1.0	0.0	0.0
	Antimony, compounds of	--	3.3	13.0
28-4-89	Delete by P.C. 1989-719 of April 28, 1989 - shall come to force on January 1, 1990			
	Atropine, Methylatropine, and their salts	1.0	0.13	0.44
	Belladonna and its preparations, on the basis of belladonna alkaloids	0.375	0.13	0.44
	Benzene (Benzol)	--	--	--
	Benzocaine	8.0	195.0	585.0
	Beta-Naphthol	--	195.0	585.0
	Revoked by P.C. 1980-1850 of July 10, 1980			
	Butacaine, its salts and derivatives when sold or recommended for ophthalmic use	0.0	0.0	0.0
	Butacaine Sulphate, except when sold or recommended for ophthalmic use	1.0	0.0	0.0
24-7-85	Cadexomer Iodine	0.0	0.0	0.0
	Cantharides, cantharidin, and their preparations, on the basis of cantharidin, except blisters	0.03	0.0	0.0
	Cantharides, blisters only	0.2	0.0	0.0
	Cedar Oil	25.0	0.0	0.0
	Revoked by P.C. 1980-1850 of July 10, 1980			
	Chlorbutol (not more often than every 4 hours)	--	325.0	975.0
2-2-84	Choline Salicylate	--	870.0	5.22g
24-7-85	Cinchocaine Hydrochloride, except suppositories	1.0	0.0	0.0
	Cinchocaine Hydrochloride, suppositories only	--	11.0	11.0
	Colchicine and its salts	--	0.55	1.65
	Colchicum and its preparations, on the basis of colchicine	--	0.27	0.81
	Croton Oil	10.0	0.0	0.0
28-4-89	Delete by P.C. 1989-719 of April 28, 1989 - shall come to force on January 1, 1990			
4-5-78	Revoked by P.C. 1978-1515 of May 4, 1978			
13-8-69	Cyproheptadine and its salts when sold or recommended for the promotion of weight gain	--	0.0	0.0
	Ephedrine and its salts	--	11.0	32.5
	Ephedrine and its salts, sprays	1.0	--	--
	Epinephrine and its salts, sprays	1.0	--	--
	Revoked by P.C. 1980-1850 of July 10, 1980			
	Gelseminine (Gelsemine) and its salts (not to be repeated within 4 hours)	--	0.55	1.65
	Gelsemium and its preparations, on the basis of the crude drug	--	16.2	48.6
	Hydrocyanic (Prussic) Acid as 2 per cent solution	--	0.062ml	0.31ml
23-11-89	Hydroquinone	2.0	--	--
	Hyoscine (Scopolamine) and its salts	0.5	0.325	0.975
	Hyoscine aminoxide hydrobromide	0.5	0.325	0.975
	Hyoscyamine and its salts	--	0.325	0.975
28-4-89	Hyoscyamus and its preparations, on the basis of hyoscyamus alkaloids	--	0.073	0.22
	Delete by P.C. 1989-719 of April 28, 1989 - shall come to force on January 1, 1990			

TABLE OF LIMITS OF DRUG DOSAGE FOR ADULTS -- Concluded

	Item	*External Use* --- *Maximum Limit*	*Internal Use* --- *Maximum Dosage* *Unless otherwise stated, doses are in milligrams*	
		Per cent	*Single*	*Daily*
	Lobelia and its preparations, on the basis of the crude drug	--	130.0	390.0
18-9-58	Lobeline and its salts	--	2.0	6.0
2-2-84	Magnesium Salicylate	--	650.0	4.0g
28-4-89	Delete by P.C. 1989-719 of April 28, 1989 - shall come to force January 1, 1990			
2-2-84	Methyl Salicylate	30.0	--	--
	Methylene Blue	--	130.0	390.0
	Revoked by P.C. 1980-1850 of July 10, 1980			
28-4-89	Delete by P.C. 1989-719 of April 28, 1989 - shall come to force January 1, 1990			
	Phenacetin	--	650.0	1.95gm
18-2-66	Phenazone and compounds thereof	--	325.0	975.0
	Phenol	2.0	32.5	260.0
18-9-58	Phenylpropanolamine when sold or recommended as an appetite depressant	--	0.0	0.0
	Phosphorus	--	0.0	0.0
28-2-64	Podophyllin	0.0	0.0	0.0
	Potassium Chlorate	--	325.0	975.0
	Potassium Chlorate, gargle	2.5	--	--
	Procaine and its salts	--	--	--
24-7-85	Proxymetacaine, its salts and derivatives when sold or recommended for ophthalmic use	0.0	0.0	0.0
28-4-89	Delete by P.C. 1989-719 of April 28, 1989 - shall come to force January 1, 1990			
	Revoked by P.C. 1984-337 of February 2, 1984			
	Salicylamide	--	975.0	2.925gm
	Santonin	--	65.0	130.0
26-6-76	Selenium and its compounds	2.5	0.0	0.0
28-4-89	Delete by P.C. 1989-719 of April 28, 1989 - shall come to force January 1, 1990			
	Delete by P.C. 1989-719 of April 28, 1989 - shall come to force January 1, 1990			
	Sodium Chlorate	--	325.0	975.0
16-7-59	Sodium Fluoride	--	0.1	0.1
28-4-89	Delete by P.C. 1989-719 of April 28, 1989 - shall come to force January 1, 1990			
2-2-84	Sodium Salicylate	--	650.0	4.0g
	Squill and its preparations, on the basis of the crude drug	--	32.5	97.5
	Stramonium and its preparations, on the basis of stramonium alkaloids	--	0.16	0.65
1-10-68	Strychnine and its salts	--	0.0	0.0
29-6-76	Tannic Acid	--	150.0	1000.0
24-7-85	Tetracaine, its salts and derivatives when sold or recommended for ophthalmic use	0.0	0.0	0.0
16-7-59	Thiocyanates	0.0	0.0	0.0
	Urethane	0.0	0.0	0.0

Where drugs having similar physiological actions occur in combination, the dosage of each shall be proportionately reduced.

Accurate dosages may be expressed in either metric units or imperial units. If the dosage is expressed in both systems, then an approximation may be used for one expression, but such approximation must precede or follow the accurate statement by which the product will be judged and must be in brackets.

C.01.022. Notwithstanding C.01.021 (b), the recommended single and daily dosage of a drug

(a) intended to be burned and the smoke inhaled may be increased to ten times the oral dose, and
(b) intended for use as suppositories may be increased to 33 1/3 per cent in excess of the oral dose.

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C.01.024. (1) Sections C.01.021 and C.01.022 do not apply to

(a) a drug sold to a drug manufacturer; or
(b) a drug sold on prescription.

(2) Paragraph C.01.021 (c) does not apply to

(a) acetaminophen;
(b) acetylsalicylic acid;
(c) magnesium salicylate;
(d) sodium salicylate; or
(e) choline salicylate.

(3) Where a drug mentioned in any of paragraphs (2)(a) to (d) is recommended for children, no person shall sell the drug for human use unless both the inner and the outer labels carry a statement that it is recommended

(a) that the drug be used as directed by a physician; or
(b) that the maximum doses of the drug not exceed the amounts set out in the following table and that single doses not be administered more frequently than every four hours.

TABLE

MAXIMUM DOSE

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Item	*Column I* *Age*	*Column II* *Maximum Children's Dose (80 mg units) Acetami-nophen Drops*	*Column III* *Maximum Children's Dose (80 mg units)*	*Column IV* *Maximum Children's Dose (160 mg units Acetami-nophen*	*Column V* *Maximum Adults Dose (325 mg units*	*Column VI* *Maximum Single Dose (mg)*	*Column VII* *Maximum Daily Dose (mg)*
1.	11 to under 12 years	--	6	3	1.5	480	2400
2.	9 to under 11 years	--	5	2.5	1.25	400	2000
3.	6 to under 9 years	--	4	2	1	320	1600
4.	4 to under 6 years	--	3	1.5	--	240	1200
5.	2 to under 4 years	--	2	1	--	160	800
6.	1 to under 2 years	1.5 or as directed by a physician	--	--	--	120	600
7.	4 months to under 1 year	1 or as directed by a physician	--	--	--	80	400
8.	0 to under 4 months	0.5 or as directed by a physician	--	--	--	40	200

(4) Where choline salicylate is recommended for children, no person shall sell the drug for human use unless both the inner and the outer labels carry a statement that it is recommended

(a) that the drug be used as directed by a physician; or
(b) that the maximum doses of the drug not exceed the amounts set out in the following table and that single doses not be administered more frequently than every four hours.

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TABLE

MAXIMUM DOSE

Age (Years)	*Adult Dosage Units (435 mg)*	*Single Dose (mg)*	*Maximum Daily Dose (mg)*
11 to under 12	1 1/2	660	3 300
9 to under 11	1 1/4	550	2 750
6 to under 9	1	440	2 200
4 to under 6	3/4	330	1 650
2 to under 4	1/2	220	1 100
Under 2	As directed by physician		

C.01.025. Both the inner and the outer labels of a drug that carry a recommended single or daily dosage or a statement of concentration in excess of the limits provided by C.01.021 shall carry a caution that the product is to be used only on the advice of a physician.

C.01.026. The provisions of C.01.025 do not apply to

(a) a drug sold on prescription, or
(b) the inner label of a single-dose container.

C.01.027. (1) Where a person advertises to the general public a drug for human use, the person shall not make any representation other than with respect to the brand name, proper name, common name, price and quantity of the drug if it

(a) contains a drug set out in the table to section C.01.021; and
(b) carries on its label
20-4-93
(i) a statement of the recommended single or daily adult dosage that results in a single or daily adult dosage of the drug referred to in paragraph (a) in excess of the maximum dosage set out in the table to section C.01.021 for that drug, or
(ii) a statement that shows a concentration of the drug referred to in paragraph (a) in excess of the maximum limit set out in the table to section C.01.021 for that drug.

(2) Subsection (1) does not apply to products containing
(a) acetaminophen;
2-6-94
(b) acetylsalicylic acid;
(c) choline salicylate;
(d) magnesium salicylate; or
(e) sodium salicylate.

4-8-93
(3) Where a person advertises to the general public a drug for human use that contains acetylsalicylic acid, the person shall not make any representation with respect to its administration to or use by children or teenagers.

Cautionary Statements and Child Resistant Packages

C.01.028. (1) Subject to subsection (2), the inner and outer labels of a drug that contains

10-1-86
(a) acetylsalicylic acid or any of its salts or derivatives, salicylic acid or a salt thereof, or salicylamide, where the drug is recommended for children, shall carry a cautionary statement to the effect that the drug should not be administered to a child under two years of age except on the advice of a physician;
(b) boric acid or sodium borate as a medicinal ingredient shall carry a cautionary statement to the effect that the drug should not be administered to a child under three years of age;
(c) hyoscine (scopolamine) or a salt thereof shall carry a cautionary statement to the effect that the drug should not be used by persons suffering from glaucoma or where it causes blurring of the vision or pressure pain within the eye;
4-8-93
(d) phenacetin, either singly or in combination with other drugs, shall carry the following cautionary statement: "CAUTION: May be injurious if taken in large doses or for a long time. Do not exceed the recommended dose without consulting a physician"; or
(e) acetylsalicylic acid for internal use shall carry a cautionary statement to the effect that the drug should not be administered to or used by children or teenagers who have chicken pox or manifest flu symptoms before a physician or pharmacist is consulted about Reye's syndrome, which statement shall also refer to the fact that Reye's syndrome is a rare and serious illness.

(2) Subsection (1) does not apply to a drug that is

(a) intended for parenteral use only;
10-1-86
(b) dispensed pursuant to a prescription; or
(c) required to be sold on prescription pursuant to these Regulations or pursuant to the Narcotic Control Regulations.

C.01.029. (1) Subject to subsections C.01.031.2(1) and (2), the inner and outer labels of a drug

(a) that contains
  (i) salicylic acid, a salt thereof or salicylamide,
  (ii) acetylsalicylic acid, or any of its salts or derivatives,
10-1-86 (iii) acetaminophen, or
  (iv) more than 5 per cent alkyl salicylates, or
(b) that is in a package that contains
23-9-93 (i) more than the equivalent of 250 mg of elemental iron, or
  (ii) more than the equivalent of 120 mg of fluoride ion, unless the drug is intended solely for use in dentists' offices,

shall carry a cautionary statement to the effect that the drug should be kept out of the reach of children.

(2) Subject to subsections C.01.031.2(1) and (2), the inner and outer labels of a drug that is in a package that contains

28-8-90 (a) more than 1.5 g of salicylic acid or the equivalent quantity of any of its salts or salicylamide,
(b) more than 2 g of acetylsalicylic acid or the equivalent quantity of any of its salts or derivatives,
(c) more than 3.2 g of acetaminophen,
(d) more than the equivalent of 250 mg of elemental iron, or
23-9-93 (e) more than the equivalent of 120 mg of fluoride ion, unless the drug is intended solely for use in dentists' offices,

shall carry a cautionary statement to the effect that there is enough drug in the package to seriously harm a child,

30-7-87 (3) The cautionary statements required under subsections (1) and (2) shall be preceded by a prominently displayed symbol that is octagonal in shape, conspicuous in colour and on a background of a contrasting colour.

C.01.030. Subject to subsections C.01.031.2(1) and (2), the inner and outer labels of a drug for use in humans

(a) that is represented as containing in each dosage unit more than 15 mg of elemental iron, or
(b) for which the largest recommended daily dose of the drug would result in an intake of more than 15 mg of elemental iron,
10-1-86 shall carry a cautionary statement to the effect that the drug is for therapeutic use only.

C.01.031. (1) Subject to section C.01.031.2,

(a) no person shall sell a drug described in subsection C.01.029(1) unless
  (i) where the drug is recommended solely for children, it is packaged in a child resistant package, or
  (ii) where the drug is not recommended solely for children, at least one of the sizes of packages available for sale is packaged in a child resistant package; and
18-12-86 (b) where a drug described in subsection C.01.029(1) is packaged in a package that is not a child resistant package, the outer label shall carry a statement that the drug is available in a child resistant package.

23-9-93 (2) Revoked by P.C. 1993-1805 of September 30, 1993

30-7-87 **C.01.031.2.** (1) Sections C.01.029 to C.01.031 do not apply to a drug that is

(a) required by these Regulations or the Narcotic Control Regulations to be sold on prescription;
(b) intended for parenteral use only;
10-1-86 (c) in effervescent or powder form;
(d) in suppository form;
(e) intended for topical use, unless it is a liquid preparation containing more than 5 per cent alkyl salicylates;
(f) packaged in a non-reclosable package containing not more than two adult standard dosage units per package, or
23-9-93 (g) in toothpaste form.

(2) Sections C.01.029 to C.01.031 do not apply to a drug that is repackaged by a pharmacist or practitioner at the time of sale.

(3) Section C.01.031 does not apply to a drug that is

(a) sold only in containers that have roll-on or spray applicators or permanently installed wick applicators;
(b) sold for exclusive use in animals other than household pets, or
23-9-93 (c) intended solely for use in dentists' offices, or packaged for hospital use only.

C.01.032. No person shall sell a corticosteroid drug for ophthalmic use unless

28-2-64 (a) the outer label or the package insert carries, as part of the directions for use, the following statements:
"Contraindications
Viral Diseases of the cornea and conjunctiva;
Tuberculosis of the eye;
Fungal disease of the eye;
Acute purulent untreated infections of the eye, which, like other diseases caused by microorganisms, may be masked or enhanced by the presence of the steroid.
Side Effects
Extended ophthalmic use of corticosteroid drugs may cause increased intraocular pressure in certain individuals and in those diseases causing thinning of the cornea, perforation has been known to occur"; and
18-6-64 (b) the inner label carries the statements required by paragraph (a) or instructions to see the outer label or package insert for information about contraindications and side effects.

C.01.033. Section C.01.032 does not apply to a corticosteroid drug that is dispensed by a registered pharmacist pursuant to a prescription.

28-2-64 **C.01.034.** No person shall disseminate to a practitioner promotional literature about corticosteroid drugs for ophthalmic use unless the statements required by section C.01.032 (a) are included in the literature.

C.01.035. Sections C.01.032 and C.01.034 do not apply to a drug sold solely for veterinary use.

10-1-86 **Miscellaneous**

C.01.036. (1) No manufacturer or importer shall sell

(a) a drug that contains phenacetin in combination with any salt or derivative of salicylic acid;
4-5-78 (b) a drug for human use that contains
(i) oxyphenisatin,
(ii) oxyphenisatin acetate,
(iii) phenisatin, or
(c) a drug for human use that contains mercury or a salt or derivative thereof, unless the drug is
(i) a drug described in Schedule C or D to the Act, or
(ii) one of the following drugs, namely,
(A) an ophthalmic drug or other drug to be used in the area of the eye,
(B) a drug for nasal administration,
(C) a drug for optic administration, or
28-4-89 (D) a drug for parenteral administration that is packaged in a multi-dose container,
in which the mercury or the salt or derivative thereof is present as a preservative and the manufacturer or importer has submitted evidence to the Director demonstrating that the only satisfactory way to maintain the sterility or stability of the drug is to use that preservative.

(2) For the purpose of clause (1)(c)(ii)(A), "area of the eye" means the area bounded by the supraorbital and infraorbital ridges and includes the eyebrows, the skin underlying the eyebrows, the eyelids, the eyelashes, the conjunctival sac of the eye, the eyeball and the soft tissue that lies below the eye and within the infraorbital ridge.

(3) Subsections (1) and (2) shall come into force on January 1, 1990.

16-11-78 **C.01.036.1.** No person shall sell, or advertise for sale, nitrous oxide to the general public.

C.01.037. (1) No person shall sell to the general public a drug that is recommended solely for children if the package in which the drug is sold contains

16-6-88 (a) more than 1.92 g of salicylamide or salicylic acid or the equivalent quantity of a salt of salicylic acid;
28-8-90 (b) more than 1.92 g of acetylsalicylic acid or the equivalent quantity of a salt or derivative thereof;
(c) more than 3.2 g of acetaminophen in 160 mg dosage units; or
(d) more than 1.92 g of acetaminophen in 80 mg dosage units.

10-1-85 (2) Subsection (1) does not apply to a drug dispensed pursuant to a prescription.

C.01.038. A drug for human use is adulterated if it contains

(a) Strychnine or any of its salts; or
(b) extracts or tinctures of
(i) *Strychnos nux vomica*,
28-6-79 (ii) *Strychnos Ignatii*, or
10-3-88 (iii) a *Strychnos* species containing strychnine, other than those species mentioned in subparagraph (i) and (ii);
(c) Methapyrilene or any of its salts,
(d) Echimidine or any of its salts; or
(e) any of the following plant species or extracts or tinctures thereof:
10-3-88 (i) *Symphytum asperum*,
(ii) *Symphytum x uplandicum*, or
(iii) any other plant species containing echimidine.

19-12-96 **C.01.039.** In *vitro* diagnostic products that are or contain drugs other than drugs listed in Schedule E to the Act, and drugs listed in Schedule D to the Act that are labelled for veterinary use only, are exempt from the application of this Part.

28-4-89 **C.01.040.** No manufacturer or importer shall sell a drug for human use that contains as an ingredient
(a) chloroform; or
(b) arsenic or any of its salts or derivatives.

19-11-92 **C.01.040.1.** No manufacturer shall use methyl salicylate as a medicinal ingredient in a drug for internal use in humans.

Colouring Agents

C.01.040.2. (1) No manufacturer shall use a colouring agent in a drug other than a colouring agent listed in subsections (3) and (4).

(2) No person shall import for sale a drug that contains a colouring agent other than a colouring agent listed in subsections (3) and (4).

(2.1) In subsections (3) and (4),

"C.I. (indication of the number)" means the designation used to identify a colouring agent in the *Colour Index* published by The Society of Dyers and Colourists, as amended from time to time; (*C.I. (indication du numéro)*)
30-8-95 "D & C (indication of the colour and the number)" means the designation used to identify, in accordance with the *Code of Federal Regulations* of the United States, a colouring agent that can be used in the United States in drugs and cosmetics; (*D&C (indication de la couleur et du numéro)*)
"FD & C (indication of the colour and the number)" means the designation used to identify, in accordance with the *Code of Federal Regulations* of the United States, a colouring agent that can be used in the United States in food, drugs and cosmetics. (FD&C (*indication de la couleur et du numéro)*)

(3) The following colouring agents are permitted in drugs for internal and external use, namely,

(a) ACID FUCHSIN D (D&C Red No. 33; C.I. No. 17200),
ALIZARIN CYANINE GREEN F (D&C Green No. 5; C.I. No. 61570),
ALLURA RED AC (FD&C Red No. 40; C.I. No. 16035),
AMARANTH (Delisted FD&C Red No. 2; C.I. No. 16185),
30-8-95 ANTHOCYANIN DERIVED FROM JUICE EXPRESSED FROM FRESH EDIBLE FRUITS OR VEGETABLES,
β-APO-8'-CAROTENAL (C.I. No. 40820),

BRILLIANT BLUE FCF SODIUM SALT (FD&C Blue No. 1; C.I. No. 42090),
BRILLIANT BLUE FCF AMMONIUM SALT (D&C Blue No. 4; C.I. No. 42090),
CANTHAXANTHIN (C.I. No. 40850),
CARAMEL,
CARBON BLACK (C.I. No. 77266),
CARMINE (C.I. No. 75470),
CARMOISINE (Delisted Ext. D&C Red No. 10; C.I. No. 14720),
β-CAROTENE (C.I. No. 40800),
CHLOROPHYLL (C.I. No. 75810),
EOSIN YS ACID FORM (D&C Red No. 21; C.I. No. 45380:2),
EOSIN YS SODIUM SALT (D&C Red No. 22; C.I. No. 45380),
ERYTHROSINE (FD&C Red No. 3; C.I. No. 45430),
FAST GREEN FCF (FD&C Green No. 3; C.I. No. 42053),
FLAMING RED (D&C Red No. 36; C.I. No. 12085),
HELINDONE PINK CN (D&C Red No. 30; C.I. No. 73360),
INDIGO (D&C Blue No. 6; C.I. No. 73000),
INDIGOTINE (FD&C Blue No. 2; C.I. No. 73015),
IRON OXIDES (C.I. Nos. 77489, 77491, 77492, 77499),
LITHOL RUBIN B SODIUM SALT (D&C Red No. 6; C.I. No. 15850),
LITHOL RUBIN B CALCIUM SALT (D&C Red No. 7; C.I. No. 1580:1),
PHLOXINE B ACID FORM (D&C Red No. 27; C.I. No. 45410:1),
PHLOXINE B SODIUM SALT (D&C Red No. 28; C.I. No. 45410),
PONCEAU 4R (C.I. No. 16255),
PONCEAU SX (FD&C No. 4; C.I. No. 14700),
QUINOLINE YELLOW WS (D&C Yellow No. 10; C.I. No. 47005),
RIBOFLAVIN,
SUNSET YELLOW FCF (FD&C Yellow No. 6; C.I. No. 15985),
TARTRAZINE (FD&C Yellow No. 5; C.I. No. 19140),
TITANIUM DIOXIDE (C.I. No. 77891);

(b) preparations made by extending any of the colouring agents listed in paragraph (a) on a substratum of
(i) alumina,
(ii) blanc fixe,
(iii) gloss white,
(iv) clay,
(v) zinc oxide,
(vi) talc,
(vii) rosin,
29-5-86 (viii) aluminum benzoate,
(ix) calcium carbonate, or
(x) any combination of the substances listed in subparagraphs (i) to (ix); and

(c) preparations made by extending any sodium, potassium, aluminum, barium, calcium, strontium or zirconium salt of any of the colouring agents listed in paragraph (a) on a substratum of
(i) alumina,
(ii) blanc fixe,
(iii) gloss white,
(iv) clay,
(v) zinc oxide,
(vi) talc,
(vii) rosin,
(viii) aluminum benzoate,
(ix) calcium carbonate, or
(x) any combination of the substances listed in subparagraphs (i) to (ix).

(4) The following colouring agents are permitted in drugs for external use, namely,

3-10-02 (a) ACID VIOLET 43 (Ext. D & C Violet No. 2; C.I. No. 60730),
ALIZUROL, PURPLE SS (D&C Violet No. 2; C.I. No. 60725),
ANNATTO (C.I. No. 75120),
30-8-95 BISMUTH OXYCHLORIDE (C.I. No. 77163),
CHROMIUM HYDROXIDE GREEN (PIGMENT GREEN 18 (C.I. No. 77289)),
DEEP MAROON (D&C Red No. 34; C.I. No. 15880:1),
DIBROMOFLUORESCEIN (SOLVENT RED 72 (C.I. No. 45370:1); ORANGE No. 5 (D & C Orange No. 5)),
30-8-95 GUANINE (C.I. No. 75170),
MANGANESE VIOLET (C.I. No. 77742),
MICA (C.I. No. 77019),

ORANGE II (D&C Orange No. 4; C.I. No. 15510),
29-5-86 PYRANINE CONCENTRATED (D&C Green No. 8; C.I. No. 59040),
QUINIZARIN GREEN SS (D&C Green No. 6; C.I. No. 61565),
TONEY RED (D&C Red No. 17; C.I. No. 26100),
URANINE ACID FORM (D&C Yellow No. 7; C.I. No. 45350:1),
URANINE SODIUM SALT (D&C Yellow No. 8; C.I. No. 45350),
30-8-95 ZINC OXIDE (C.I. No. 77947);

(b) preparations made by extending any of the colouring agents listed in paragraph (a) on a substratum of
(i) alumina,
(ii) blanc fixe,
(iii) gloss white,
(iv) clay,
(v) zinc oxide,
(vi) talc,
(vii) rosin,
(viii) aluminum benzoate,
(ix) calcium carbonate, or
(x) any combination of the substances listed in subparagraphs (i) to (ix); and

(c) preparations made by extending any sodium, potassium, aluminum, barium, calcium, strontium or zirconium salt of any of the colouring agents listed in paragraph (a) on a substratum of
(i) alumina,
(ii) blanc fixe,
29-11-84 (iii) gloss white,
(iv) clay,
(v) zinc oxide,
(vi) talc,
(vii) rosin,
(viii) aluminum benzoate,
(ix) calcium carbonate, or
(x) any combination of the substances listed in subparagraphs (i) to (ix).

(5) Subsections (1) and (2) do not apply in respect of a drug that is represented as being solely for use in the disinfection, for disease prevention, of
23-6-94

(a) medical devices;
(b) health care facilities; or
(c) premises in which food is manufactured, prepared or kept.

Schedule F Drugs

10-7-80 **C.01.041.** (1) In this section and sections C.01.041.1 to C.01.046, "Schedule F Drug" means a drug listed or described in Schedule F to these Regulations.

(1.1) Subject to sections C.01.043 and C.01.046, no person shall sell a substance containing a Schedule F drug unless

4-8-93 (a) the sale is made pursuant to a verbal or written prescription received by the seller; and
(b) where the prescription has been transferred to the seller under section C.01.041.1, the requirements of section C.01.041.2 have been complied with.

(2) Where the prescription for a Schedule F Drug is written, the person selling the drug shall retain the prescription for at least two years from the date of filling.

(3) Where the prescription for a Schedule F Drug is verbal, the person to whom the prescription is communicated by the practitioner shall forthwith reduce the prescription to writing and the person selling the drug shall retain that written prescription for a period of at least two years from the date of filling.

(4) The person reducing a verbal prescription to writing shall indicate on the written prescription

25-3-65 (a) the date and number of the prescription;
(b) the name and address of the person for whose benefit the prescription is given;
20-4-93 (c) the proper name, common name or brand name of the specified drug and the quantity thereof;
(d) his name and the name of the practitioner who issued the prescription; and
(e) the directions for use given with the prescription, including whether or not the practitioner authorized the refilling of the prescription and, if the prescription is to be refilled, the number of times it may be refilled.

4-5-78 (5) Subsections (1.1) to (4) do not apply to a substance containing

(a) chloral hydrate in preparations for external use, where it constitutes not more than 1% of the substance,
9-5-72 or
(b) hexachlorophene and its salts, where it constitutes not more than 0.75% of the substance, calculated as hexachlorophene.

C.01.041.1 A pharmacist may transfer to another pharmacist a prescription for a Schedule F Drug.

4-5-78 **C.01.041.2** A pharmacist to whom a prescription has been transferred under section C.01.041.1 shall not sell a drug pursuant thereto until

(a) he has obtained from the pharmacist transferring the prescription his name and address, the number of authorized refills remaining and the date of the last refill; and
(b) he has
(i) received a copy of the prescription as written by the practitioner or as reduced to writing as required by subsections C.01.041(3) and (4), as the case may be, or
(ii) where the prescription has been transferred to him verbally, reduced the prescription to writing indicating therein the information specified in subsection C.01.041(4).
4-5-78

C.01.041.3 The pharmacist to whom a prescription for a Schedule F Drug is transferred under section C.01.041.1 shall retain in his files for a period of two years the information and documents referred to in section C.01.041.2.

C.01.041.4 A pharmacist who transfers a prescription under section C.01.041.1

(a) shall enter on the original of the prescription or in a suitable record of prescriptions kept under the name of each patient, the date of transfer; and
(b) shall not make any further sales under the prescription nor transfer it to another pharmacist.

25-3-65 **C.01.042.** (1) No person shall refill a prescription for a Schedule F Drug unless the practitioner so directs and no person shall refill such a prescription more times than the number of times prescribed by the practitioner.

(2) The person filling or refilling a prescription for a Schedule F Drug shall enter on the original of the prescription or in a suitable record of prescriptions kept under the name of each patient
4-5-78 (a) the date of filling;
(b) the date of each refill, if applicable;
(c) the quantity of drug dispensed at the original filling and each refill; and
(d) his name.

C.01.043. (1) A person may sell a Schedule F Drug, without having received a prescription therefor, to
(a) a drug manufacturer;
(b) a practitioner;
(c) a wholesale druggist;
(d) a registered pharmacist;
25-3-65 (e) a hospital certified by the Department of National Health and Welfare;
(f) a Department of the Government of Canada or of a province, upon receipt of a written order signed by the Minister thereof or his duly authorized representative; or
(g) any person, upon receipt of a written order signed by the Director.

(2) Where a person makes a sale authorized by paragraph (f) or (g) of subsection (1), he shall retain the written order for the drug for a period of at least two years from the date of filling the order.

20-4-93 **C.01.044.** (1) Where a person advertises to the general public a Schedule F Drug, the person shall not make any representation other than with respect to the brand name, proper name, common name, price and quantity of the drug.

(2) Subsection (1) does not apply where
(a) the drug is listed in Part II of Schedule F; and
4-8-93 (b) the drug is
(i) in a form not suitable for human use, or
(ii) labelled in the manner prescribed by paragraph C.01.046(b).

C.01.045. (1) Subject to subsection (2), no person other than

(a) a practitioner;
(b) a drug manufacturer;
(c) a wholesale druggist;
5-3-65 (d) a registered pharmacist; or
(e) a resident of a foreign country while a visitor in Canada,
shall import a Schedule F Drug.

4-8-93 (2) Any person may import a Schedule F Drug listed in Part II of Schedule F if the drug is imported in such form or so labelled that it could be sold by that person pursuant to section C.01.046.

C.01.046. A person may sell a drug listed or described in Part II of Schedule F to the Regulations, without having received a prescription therefor, if

(a) the drug is in a form not suitable for human use; or
17-5-01 (b) the principal display panel of both the inner label and the outer label carries, in both official languages, the statement "For Veterinary Use Only/Pour usage vétérinaire seulement" or "Veterinary Use Only/Usage vétérinaire seulement", immediately following or preceding the brand name, proper name or common name, in type size not less than one-half as large as the largest type on the label.

C.01.047. Revoked by P.C. 1980-1849 of July 10, 1980

20-4-93 **C.01.048.** (1) Where a person who is a physician, dentist, veterinary surgeon or pharmacist registered and entitled to practise that person's profession in a province has signed an order specifying the brand name, proper name or common name and the quantity of a drug, other than

14-5-97 (a) a narcotic as defined in the *Narcotic Control Regulations*,
(b) a controlled drug as defined in subsection G.01.001(1), or
(c) a new drug in respect of which a notice of compliance has not been issued under section C.08.004,

4-10-73 the person who receives the order may distribute the drug to the physician, dentist, veterinary surgeon or pharmacist as a sample if the drug is labelled in accordance with these Regulations.

(2) An order referred to in subsection (1) may provide that the order be repeated at specified intervals during any period not exceeding six months.

C.01.049. A person who, under section C.01.048, distributes a drug as a sample shall

(a) maintain records showing
(i) the name, address and description of each person to whom the drug is distributed,
20-4-93 (ii) the brand name, quantity and form of the drug distributed, and
(iii) the date upon which each such distribution was made; and

25-7-63 (b) keep those records and all orders received for drugs in accordance with section C.01.048 for a period of not less than two years from the date upon which the distribution referred to in the records was made.

Recalls

21-5-82 **C.01.051.** Where a manufacturer who sells a drug in dosage form or a person who imports into and sells in Canada a drug in dosage form commences a recall of the drug, the manufacturer or importer shall forthwith submit to the Director the following information:

20-4-93 (a) the proper name of the drug, the common name of the drug if there is no proper name, the brand name of the drug and the lot number;
(b) in the case of an imported drug, the names of the manufacturer and importer;
(c) the quantity of the drug manufactured or imported;
21-5-82 (d) the quantity of the drug distributed;
(e) the quantity of the drug remaining on the premises of the manufacturer or importer;
(f) the reasons for initiating the recall; and
(g) a description of any other action taken by the manufacturer or importer with respect to the recall.

C.01.052. Revoked by P.C. 1982-524 of May 21, 1982.

21-5-82 **C.01.055.** Revoked by P.C. 1982-524 of May 21, 1982.

C.01.056. Revoked by P.C. 1982-524 of May 21, 1982.

Limits of Variability

C.01.061. (1) Where the net amount of a drug in a package is not expressed on the label in terms of number of dosage units, any 10 packages of the drug selected as provided by official method DO-31, Determination of Net Contents, dated December 7, 1988, shall contain an amount of the drug such that, when determined by that official method, the average of the net amounts of the drug in the 10 packages is not less than the net amount of the drug shown on the label.

(2) Where the net amount of a drug in a package is expressed on the label in terms of the number of dosage units, any 10 packages of the drug selected as provided by official method DO-31, Determination of Net Contents, dated December 7, 1988, shall contain a number of units such that, when determined by that official method,
(a) the average number of dosage units in the 10 packages is not less than the number of dosage units shown on the label;
(b) no package contains less than the number of dosage units shown on the label except as provided in the table; and
14-5-97 (c) where the drug is a controlled drug as defined in subsection G.01.001(1) or a narcotic as defined in the *Narcotic Control Regulations*, no package contains more than the number of dosage units shown on the label except as provided in the table to this section.

21-9-89 **TABLE**

Item	Column I Labelled Number of Dosage Units Per Package	Column II Permitted Variation from the Labelled Number
1.	50 or less	0
2.	More than 50, but less than 101	1
3.	101 or more	the greater of 1 unit or 0.75% of the labelled number, rounded up to the next whole number

1-11-94 **C.01.062.** (1) Subject to subsections (2) to (5), no manufacturer shall sell a drug in dosage form where the amount of any medicinal ingredient therein, determined using an acceptable method, is

7-11-95 (a) less than 90.0 per cent of the amount of the medicinal ingredient shown on the label; or
(b) more than 110.0 per cent of the amount of the medicinal ingredient shown on the label.

1-11-94 (2) Subject to subsection (5), where a drug in dosage form contains a medicinal ingredient that is a volatile substance of botanical origin or its synthetic equivalent, the amount of that ingredient, determined using an acceptable method, shall be

20-2-92 (a) not less than 85.0 per cent of the amount of the medicinal ingredient shown on the label; and

(b) not more than 120.0 per cent of the amount of the medicinal ingredient shown on the label.

(3) Subject to subsection (5), where a drug in capsule form contains a medicinal ingredient that is a vitamin in a fish-liver oil, no variation from the amount of the medicinal ingredient as shown on the label, determined using an acceptable method, is permitted other than that which is in accordance with the variation for that fish-liver oil as stated in any publication whose name is referred to in Schedule B to the Act.

(4) Subject to subsection (5), where a drug in dosage form contains a medicinal ingredient that is a vitamin, no variation from the amount of the medicinal ingredient shown on the label, determined using an acceptable method, is permitted other than the variation set out in column III or IV of an item of the table to this section opposite the vitamin set out in column I of that item for the amount of vitamin set out in column II of that item.

(5) Subsections (1) to (4) do not apply in respect of

(a) a drug for which a notice of compliance has been issued pursuant to section C.08.004;

26-8-98 (b) Repealed by P.C. 1998-1461 of August 26, 1998.

20-2-92 (c) a drug for which a standard is contained in any publication whose name is referred to in Schedule B to the Act;

(d) a drug described in Schedule C or D to the Act or Division 6 of Part C of these Regulations; or

(e) a drug for which a drug identification number has been assigned under subsection C.01.014.2(1) and in respect of which

(i) the conditions of pharmaceutical production and quality control are suitable for controlling the identity, quality, purity, stability, safety, strength and potency of the drug,

26-8-98 (ii) all labels, package inserts, product brochures and file cards to be used in connection with the drug make proper claims in respect of the drug,

(iii) the drug can, without undue foreseeable risk to humans, be used for the purposes and under the conditions of use recommended by the manufacturer, and

(iv) the drug is effective for the purposes and under the conditions of use recommended by the manufacturer.

TABLE

Item	*Column I* *Vitamin*	*Column II* *Recommended daily dose*	*Column III* *Limits of variation when the recommended daily dose shown on label is equal to or less than amount set out in column II*	*Column IV* *Limits of variation when the recommended daily dose shown on label is greater than amount set out in column II*
1.	vitamin A (or as β-carotene)	10 000 I.U.	90.0 - 165.0 %	90.0 - 115.0 %
2.	thiamine	4.5 mg	90.0 - 145.0 %	90.0 - 125.0 %
3.	riboflavin	7.5 mg	90.0 - 125.0 %	90.0 - 125.0 %
4.	niacin or niacinamide	45 mg	90.0 - 125.0 %	90.0 - 125.0 %
5-10-92 5.	pyridoxine	3 mg	90.0 - 125.0 %	90.0 - 125.0 %
6.	**d**-pantothenic acid	15 mg	90.0 - 135.0 %	90.0 - 125.0 %
7.	folic acid	0.4 mg	90.0 - 135.0 %	90.0 - 115.0 %
8.	vitamin B_{12}	14 µg	90.0 - 135.0 %	90.0 - 125.0 %
9.	vitamin C	150 mg	90.0 - 145.0 %	90.0 - 125.0 %
10.	vitamin D	400 I.U.	90.0 - 145.0 %	90.0 - 115.0 %
11.	vitamin E	25 I.U.	90.0 - 125.0 %	90.0 - 125.0 %
12.	vitamin K	0.0 mg		90.0 - 115.0 %
13.	biotin	0.0 mg		90.0 - 135.0 %

7-8-96 **C.01.063.** Revoked by P.C. 1996-1223 of August 7, 1996.

C.01.064. Where a drug is prepared for ophthalmic or parenteral use and contains a preservative ingredient, that ingredient

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(a) shall be present only in an amount necessary to obtain the intended action and that does not pose undue risk to humans or animals; and
(b) shall not interfere with the therapeutic properties of the drug.

7-8-96 **C.01.065.** No person shall sell a drug that is prepared for ophthalmic or parenteral use unless a representative sample of each lot of the drug in its immediate container

20-4-93 (a) is tested by an acceptable method for identity, and the drug is found to be true to its proper name, or to its common name if there is no proper name;
(b) is tested by an acceptable method for sterility, except
(i) for living vaccines, or
7-8-96 (ii) where the manufacturer has submitted evidence, satisfactory to the Director to prove that processing controls ensure the sterility of the drug in its immediate container,
22-5-86 and the drug is found to be sterile; and
(c) is subjected to such further tests satisfactory to the Director to ensure that the drug is safe to use according to directions.

1-12-77 **C.01.066.** No person shall sell a drug in aqueous solution that is prepared for parenteral use unless it has been prepared with non-pyrogenic water produced by distillation or reverse osmosis.

C.01.067. (1) Subject to subsection (2), no person shall sell a drug that is prepared for parenteral use unless a representative sample of each lot of the drug in its immediate container

7-8-96 (a) is tested by an acceptable method for the presence of pyrogens; and
(b) when so tested, is found to be non-pyrogenic.

(2) Subsection (1) does not apply in respect of a drug that cannot be tested for the presence of pyrogens or that is inherently pyrogenic.

19-11-92 **C.01.068.** Detailed records of the tests required by sections C.01.065 and C.01.067 shall be retained by the manufacturer for a period of at least one year after the expiration date on the label of the drug.

C.01.069. The packaging of a drug that is prepared for parenteral use shall meet the following requirements:

(a) the immediate container shall be of such material and construction that
(i) no deleterious substance is yielded to the drug,
(ii) it is non-reactive with the drug,
7-8-96 (iii) visual or electronic inspection of the drug is possible,
(iv) protection against environmental factors that cause deterioration or contamination of the drug is provided or, where that protection cannot be provided by the immediate container, it is provided by the secondary packaging, and
(v) a sufficient quantity of the drug is contained to allow withdrawal of the labelled amount of the drug; and
(b) the immediate closures and any material coming into contact with the drug in its immediate container shall meet the requirements of subparagraphs (a)(i) and (ii).

C.01.070. No person shall sell a drug that is a hypodermic tablet that does not completely dissolve in and form a clear solution with water.

Mercuric Chloride Tablets

C.01.071. No person shall sell mercuric chloride tablets for household use that are packaged in lots of two hundred or less, unless

(a) such tablets are
  (i) of an irregular or angular shape,
  (ii) coloured blue, and
  (iii) packed in an immediate container that is readily distinguishable by touch, and

17-5-01 (b) the principal display panel of both the inner and the outer labels carries in prominent type and in a colour contrasting to that of such labels

  (i) the design of a skull and cross-bones, and
  (ii) the word "Poison".

C.01.081. Revoked by P.C. 1980-1850 of July 10, 1980.

C.01.085. Revoked by P.C. 1980-1850 of July 10, 1980.

Disinfectants

1-12-77 **C.01.091.** Revoked by P.C. 1977-3383 of December 1, 1977.

Synthetic Sweeteners

4-5-78 **C.01.101.** (1) Revoked by P.C. 1978-1515 of May 4, 1978.
19-10-78 (2) Revoked by P.C. 1978-3211 of October 19, 1978.
4-5-78 (3) Revoked by P.C. 1978-1515 of May 4, 1978.

C.01.121. Revoked by P.C. 1980-1850 of July 10, 1980.

C.01.122. Revoked by P.C. 1980-1850 of July 10, 1980.

Aminopyrine and Dipyrone

C.01.131. No person shall sell Aminopyrine or Dipyrone (a derivative of Aminopyrine) for oral or parenteral use, unless

(a) the inner label carries the statement:
"WARNING: Fatal agranulocytosis may be associated with the use of Aminopyrine and Dipyrone. It is essential that adequate blood studies be made. (See enclosed warnings and precautions)", and

(b) the outer label or the package insert carries the following statements:

4-10-65 "WARNING: Serious and even fatal agranulocytosis is known to occur after the administration of Aminopyrine or Dipyrone. Fatal agranulocytosis has occurred after short term, intermittent and prolonged therapy with the drugs. Therefore, the use of these drugs should be as brief as possible. Bearing in mind the possibility that such reactions may occur, Aminopyrine or Dipyrone should be used only when other less potentially dangerous agents are ineffective. PRECAUTIONS: It is essential that frequent white blood cell counts and differential counts be made during treatment with these drugs. However, it is emphasized that agranulocytosis may occur suddenly without prior warning. The drug should be discontinued at the first evidence of any alteration of the blood count or sign of agranulocytosis, and the patient should be instructed to discontinue use of the drug at the first indication of sore throat or sign of other infection in the mouth or throat (pain, swelling, tenderness, ulceration)."

4-10-65 **C.01.132.** No person shall disseminate to a practitioner promotional literature about Aminopyrine or Dipyrone unless the statements set out in section C.01.131 are included in such literature.

4-10-65 **C.01.133.** The provision of section C.01.131 and C.01.132 do not apply to preparations containing Aminopyrine or Dipyrone that are

(a) dispensed by a pharmacist pursuant to a prescription; or
(b) sold for veterinary use only.

Coated Potassium Salts

C.01.134. No person shall sell coated tablets containing potassium salts, with or without thiazide diuretics, unless the inner label thereof or the package insert carries the following statement:

31-1-66 "WARNING: A probable association exists between the use of coated tablets containing potassium salts, with or without thiazide diuretics, and the incidence of serious small bowel ulceration. Such preparations should be used only when adequate dietary supplementation is not practical, and should be discontinued if abdominal pain, distention, nausea, vomiting or gastro-intestinal bleeding occur."

4-10-65 **C.01.135.** No person shall disseminate to a practitioner promotional literature about coated tablets containing potassium salts, with or without thiazide diuretics, unless the statement set out in section C.01.134 is included in such literature.

C.01.136. The provisions of section C.01.134 and C.01.135 do not apply to coated tablets containing potassium salts with or without thiazide diuretics that

4-10-65 (a) are sold for veterinary use only;
(b) are dispensed by a pharmacist pursuant to a prescription; or
(c) contain 100 milligrams or less of elemental potassium per tablet.

New Drugs

C.01.301-307. Revoked by P.C. 1963-1493 of 10th October 1963.

See Division 8, Part C.

Antibiotics

C.01.401. Except as provided in these Regulations, an antibiotic for other than parenteral use shall, in addition to meeting the requirements of section C.01.004, carry on both the inner label and outer label the potency of the drug, expressed in terms of International Units where established or, if no International Unit has been established, in terms of units, milligrams, micrograms or fractions of a gram,

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(a) per gram in the case of solids or viscous liquids;
(b) per millilitre in the case of other liquids; and
(c) per individual dosage or dispensing form in the case of antibiotic preparations put up in individual dosage or dispensing form.

19-11-92 **C.01.402.** Revoked by P.C. 1992-2327 of November 19, 1992.

C.01.410. Revoked by P.C. 1980-1850 of July 10, 1980.

C.01.411. Revoked by P.C. 1980-1850 of July 10, 1980.

C.01.412. Revoked by P.C. 1980-1850 of July 10, 1980.

C.01.420. Revoked by P.C. 1980-1850 of July 10, 1980.

C.01.421. Revoked by P.C. 1980-1850 of July 10, 1980.

C.01.422. Revoked by P.C. 1980-1850 of July 10, 1980.

Chloramphenicol

C.01.430. Revoked by P.C. 1980-1850 of July 10, 1980.

C.01.431. Revoked by P.C. 1980-1850 of July 10, 1980.

C.01.432. Revoked by P.C. 1980-1850 of July 10, 1980.

C.01.433. No person shall sell chloramphenicol and its salts and derivatives, for oral or parenteral use, unless

(a) the inner label carries a warning statement to the effect that
  (i) bone marrow depression has been associated with the use of chloramphenicol, and
  (ii) the enclosed warnings and precautions should be read carefully; and

(b) the outer label or the package insert carries the following:

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  (i) a warning statement to the effect that chloramphenicol should not be used in the treatment or prophylaxis of minor infections or where it is not indicated, as in colds, influenza, or infections of the upper respiratory tract; that some degree of depression of the bone marrow is commonly seen during therapy, is dose-related and is potentially reversible; that blood studies may detect early changes and; that the other type of bone marrow depression, a sudden, delayed and usually fatal bone marrow hypoplasia that may occur without warning, is very rare, and
  (ii) a statement of precautions to be taken to the effect that it is essential that appropriate blood studies be make during treatment with chloramphenicol and that while blood studies may detect early peripheral blood changes, such studies cannot be relied on to detect the rare and generally irreversible bone marrow depression prior to development of aplastic anaemia.

24-7-61 **C.01.434.** The provisions of section C.01.433 do not apply to chloramphenicol and its salts or derivatives sold by a registered pharmacist.

24-7-61 **C.01.435.** No person shall disseminate to a practitioner promotional literature about chloramphenicol and its salts or derivatives for oral or parenteral use unless the statements set out in paragraph (b) of section C.01.433 are included in such literature.

24-7-61 **C.01.436.** The provisions of sections C.01.433 and C.01.435 do not apply to a drug sold solely for veterinary use.

C.01.440. Revoked by P.C. 1980-1850 of July 10, 1980.

C.01.441. Revoked by P.C. 1980-1850 of July 10, 1980.

C.01.442. Revoked by P.C. 1980-1850 of July 10, 1980.

Sections C.01.450, C.01.451, C.01.452, C.01.460, C.01.461, C.01.462, C.01.470, C.01.471, C.01.472, C.01.480, C.01.490, C.01.491, C.01.492, C.01.493, C.01.494, C.01.495, C.01.496, C.01.497, C.01.510, C.01.511, C.01.512, C.01.513, C.01.520, C.01.521, C.01.522, C.01.530, C.01.531, C.01.532, C.01.540, C.01.541, C.01.542, C.01.550, C.01.551, C.01.552, C.01.560, C.01.561, C.01.562, C.01.563, C.01.570, C.01.571, C.01.572, C.01.580, C.01.590, C.01.591, C.01.592 are revoked by P.C. 1980-1850 of July 10, 1980 (Pages 86, 87 and 88).

10-7-80 **C.01.600.** No person shall sell for veterinary use a drug listed in the Table of Limits of Drug Dosage for Adults, other than a drug in a form not suitable for human use, unless both the inner and outer labels carry the statement "For Veterinary Use Only" or "Veterinary Use Only".

4-8-93 **C.01.601.** Revoked by P.C. 1993-1621 of August 4, 1993.

C.01.602. The provisions of C.01.401 and C.01.402 do not apply to an antibiotic in amounts less than 50 parts per million contained in an animal food.

C.01.603. The provisions of C.01.401 (b) and (c) and C.01.402 do not apply to an antibiotic in amounts greater than 50 parts per million contained in an animal food.

10-7-80 **C.01.604.** Both the inner and outer labels of a veterinary drug represented as containing a vitamin shall carry

(a) a statement of the amount of each vitamin present in the drug, expressed in terms of the proper name only of the vitamin in
  (i) International Units per gram or per millilitre for vitamin A, provitamin A, vitamin D, and vitamin E,
  (ii) milligrams per gram in the case of solids or viscous liquids, or per millilitre in the case of other liquids, for thiamine, riboflavin, niacin, niacinamide, pyridoxine, **d**-pantothenic acid, **d**-panthenol, folic acid, ascorbic acid, and vitamin K,
  (iii) micrograms per gram in the case of solids or viscous liquids, or per millilitre in the case of other liquids, for biotin, and vitamin B_{12},
  (iv) Oral Units for vitamin B_{12} with intrinsic factor concentrate, or
  (v) for vitamin products put up in individual dosage or dispensing form, the specified units per individual dosage or dispensing form,
(b) except for drugs in a form not suitable for human use, the statement "For Veterinary Use Only" or "Veterinary Use Only".

10-7-80 **C.01.605.** An antibiotic for parenteral use that is recommended for veterinary use only shall carry on both the inner and outer labels

(a) the potency of the drug expressed in terms of International Units where established, or, if no International Unit has been established, in terms of units, milligrams or fractions of a gram, per gram in the case of solids or viscous liquids, per millilitre in the case of other liquids, or per individual dosage or dispensing form for antibiotic preparations put up in individual dosage or dispensing form, and

19-11-92 (b) Revoked by P.C. 1992-2327 of November 19, 1992;

(c) the statement "For Veterinary Use Only" or "Veterinary Use Only".

21-7-88 **C.01.606.** No person shall sell an antibiotic preparation for the treatment of animals, other than an antibiotic preparation that is a new drug sold pursuant to section C.08.013, unless,

(a) where the preparation is not to be used for lactating animals providing milk to be consumed as food, the inner and outer labels of the preparation carry a statement to that effect; or

(b) where the preparation may be used for lactating animals providing milk to be consumed as food,

21-7-88 (i) there has been submitted, on request, to the Director, acceptable evidence to show the period of time, not exceeding 96 hours, that must elapse after the last treatment with the preparation in order that the milk from treated lactating animals will contain no residue of antibiotics that would cause injury to human health, and

23-9-93 (ii) the principal display panel of the outer label of the preparation, the inner label and the packaging insert, if any, describing the antibiotic preparation carry the warning " **WARNING: MILK TAKEN FROM TREATED ANIMALS DURING TREATMENT AND WITHIN ... HOURS AFTER THE LATEST TREATMENT MUST NOT BE USED AS FOOD**", where the number of hours to be inserted is determined according to evidence submitted pursuant to subparagraph (i).

7-6-90 **C.01.606.1** No person shall sell a product intended for the prevention or treatment of foot rot of cattle if that product contains Ethylenediamine Dihydroiodide (EDDI).

10-7-80 **C.01.607.** Notwithstanding subparagraph C.01.004(1)(c)(ii), the declaration of a lot number is not required on the label of an animal feeding-stuff containing a drug.

C.01.608. The provisions of section C.01.604 do not apply to medicated feeds registered under the Feeding Stuffs Act.

2-1-58 **C.01.609.** Notwithstanding the provisions of section C.01.401(a), the potency of an antibiotic in amounts greater than 50 parts per million contained in a medicated feed registered under the Feeding Stuffs Act may be declared in grams per ton.

4-3-63 **C.01.610.** No person shall sell any substance having oestrogenic activity for administration to poultry that may be consumed as food.

C.01.610.1 No person shall sell a drug for administration to animals that produce food or that are intended for consumption as food if that drug contains

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(a) chloramphenicol or its salts or derivatives;

(b) a 5-nitrofuran compound;

20-11-97 (c) clenbuterol or its salts or derivatives;

13-8-03 (d) a 5-nitroimidazole compound; or

(e) diethylstilbestrol or other stilbene compounds.

C.01.610.2 No person shall sell an antibiotic preparation containing chloramphenicol, its salts or derivatives, for administration to animals that do not produce food and that are not intended for consumption as food unless

(a) both the inner label and outer label of the preparation carry the words "WARNING: FEDERAL LAW PROHIBITS THE ADMINISTRATION OF THIS PREPARATION TO ANIMALS THAT PRODUCE FOOD OR ANIMALS THAT ARE INTENDED FOR CONSUMPTION AS FOOD/MISE EN GARDE: EN VERTU DES LOIS FÉDÉRALES, IL EST INTERDIT D'ADMINISTRER CETTE PRÉPARATION AUX ANIMAUX QUI PRODUISENT DES ALIMENTS OU AUX ANIMAUX DESTINÉS À ÊTRE CONSOMMÉS COMME ALIMENTS";

19-9-91 (b) where the preparation is for parenteral use, the preparation contains, in the form of chloramphenicol sodium succinate, not more than one gram of chloramphenicol per vial;

(c) where the preparation is for ophthalmic use, the preparation contains not more than one per cent chloramphenicol; and

(d) where the preparation is for oral use, the preparation

(i) is in tablet or capsule form and contains not more than one gram of chloramphenicol per tablet or capsule, or

(ii) is in the form of a chloramphenicol palmitate suspension and contains not more than three grams of chloramphenicol per container.

C.01.611. (1) The Director may, in writing, from time to time require the manufacturer of a drug recommended for administration to animals that may be consumed as food

25-3-65

(a) to file with him in respect of that drug a submission, in form and content satisfactory to the Director, describing in detail tests carried out to determine that no residues of the drug, except residues within the limits prescribed by these Regulations, remain in meat, meat by-products, eggs or milk; and

23-9-93 (b) to print on the principal display panel of the outer label, the inner label and the packaging insert, if any, that describes the drug, a warning that meat, meat by-products, eggs or milk from animals to which the drug has been administered cannot be sold for consumption as food unless there has elapsed since the administration of the drug a period of time specified by the Director, based on a review of the available data with respect to drug residue.

(2) No manufacturer shall sell a drug in respect of which the Director has required a warning to be printed pursuant to paragraph (b) of subsection (1) unless the manufacturer has complied with that request.

16-8-94 **C.01.612.** Revoked by P.C. 1994-1369 of August 16, 1994.

Contraceptive Drugs

14-1-70 **C.01.625.** Contraceptive drugs that are manufactured, sold or represented for use in the prevention of conception and that are not listed in Schedule F may be advertised to the general public.

DIVISION 1A

ESTABLISHMENT LICENCES

Interpretation

C.01A.001. (1) The definitions in this subsection apply in this Division and in Divisions 2 to 4.

"batch certificate" means a certificate issued by the fabricator of a lot or batch of a drug that is exported within the framework of a mutual recognition agreement and in which the fabricator

(a) identifies the master production document for the drug and certifies that the lot or batch has been fabricated, packaged/labelled and tested in accordance with the procedures described in that document;

(b) provides a detailed description of the drug, including

(i) a statement of all properties and qualities of the drug, including the identity, potency and purity of the drug, and

3-10-02 (ii) a statement of tolerances for the properties and qualities of the drug;

(c) identifies the analytical methods used in testing the lot or batch and provides details of the analytical results obtained;

(d) sets out the addresses of the buildings at which the lot or batch was fabricated, packaged/labelled and tested; and

(e) certifies that the lot or batch was fabricated, packaged/labelled and tested in accordance with the good manufacturing practices of the regulatory authority that has recognized those buildings as meeting its good manufacturing practices standards. (*certificat de lot*)

"class monograph" means a document prepared by the Department of Health that

17-12-97 (a) lists the types and strengths of medicinal ingredients that may be contained in drugs of a specified class; and

(b) sets out labelling and other requirements that apply to those drugs. (*monographie de classe*)

"dilute drug premix" means a drug for veterinary use that results from mixing a drug premix with a feed as defined in section 2 of the *Feeds Regulations, 1983*, with the lowest approved dosage level of the drug. (*prémélange médicamenteux dilué*)

"dosage form class" means a parenteral, tablet, capsule, solution, suspension, aerosol, powder, suppository, medical gas or drug premix, or any other dosage form class designated by the Minister. (*classe de forme posologique*)

"drug premix" means a drug for veterinary use to which a drug identification number has been assigned, where the directions on its label specify that it is to be mixed with feed as defined in section 2 of the *Feeds Act*. (*prémélange médicamenteux*)

"fabricate" means to prepare and preserve a drug for the purposes of sale. (*manufacturer*)

"import" means to import into Canada a drug for the purpose of sale. (*importer*)

3-10-02 "MRA country" means a country that is a participant in a mutual recognition agreement with Canada. (*pays participant*)

3-10-02 "mutual recognition agreement" means an international agreement that provides for the mutual recognition of compliance certification for good manufacturing practices for drugs. (*accord de reconnaisance mutuelle*)

"package/label" means to put a drug in its immediate container or to affix the inner or outer label to the drug. (*emballer-étiqueter*)

"pharmaceutical" means a drug other than a drug listed in Schedule C or D to the Act. (*produit pharmaceutique*)

3-10-02 "recognized building" means, in respect of the fabrication, packaging/labelling or testing of a drug, a building that a regulatory authority that is designated under subsection C.01A.019(1) in respect of that activity for that drug has recognized as meeting its good manufacturing practices standards in respect of that activity for that drug. (*bâtiment reconnu*)

3-10-02 "regulatory authority" means a government agency or other entity in an MRA country that has a legal right to control the use or sale of drugs within that country and that may take enforcement action to ensure that drugs marketed within its jurisdiction comply with legal requirements. (*autorité réglementaire*)

3-10-02 "site" Repealed by P.C. 2002-1710 of October 3, 2002

"wholesale" means to sell any of the following drugs, other than at retail sale, where the seller's name does not appear on the label of the drugs:

3-10-02 (a) a drug listed in Schedule C or D to the Act or in Schedule F to these Regulations or a controlled drug as defined in subsection G.01.001(1); or

(b) a narcotic as defined in the *Narcotic Control Regulations*. (*vendre en gros*)

19-12-96 (2) In this Division and in Division 2, "drug" means a drug in dosage form, or a drug that is a bulk process intermediate that can be used in the preparation of a drug listed in Schedule C to the Act or in Schedule D to the Act that is of biological origin. It does not include a dilute drug premix, a medicated feed as defined in section 2 of the *Feeds Regulations, 1983*, a drug that is used only for the purposes of an experimental study in accordance with a certificate issued under section C.08.015 or a drug listed in Schedule H to the Act.

19-12-96 (3) Where the Minister designates additional dosage form classes, the Minister shall make a list of those classes available on request.

C.01A.002. (1) This Division does not apply to

(a) wholesaling a drug premix;
(b) importing or compounding, pursuant to a prescription, a drug that is not commercially available in Canada by one of the following persons, namely,
  (i) a pharmacist,
  (ii) a practitioner, and
  (iii) a person who compounds a drug under the supervision of a practioner;
7-6-01 (c) any activity with respect to a drug that is used only for the purposes of clinical testing in accordance with subsection C.05.006(1) or section C.08.005; and
17-12-97 (d) fabricating, packaging/labelling, testing as required under Division 2, distributing as a distributer referred to in section C.01A.003, wholesaling or importing any of the following drugs for which prescriptions are not required and that are for human use in dosage form and not represented as a treatment, preventative or cure for any of the diseases, disorders or abnormal physical states set out in Schedule A to the Act, namely,
  (i) homeopathic drugs,
  (ii) drugs that meet the requirements of a class monograph entitled "Vitamin Supplements", "Mineral Supplements", "Dietary Vitamin Supplements" or "Dietary Mineral Supplements", as the case may be, and
  (iii) drugs that
    (A) contain a plant, mineral or animal substance in respect of which therapeutic activity or disease prevention activity is claimed, including traditional herbal medicines, traditional Chinese medicines, ayurvedic (East Indian) medicines and traditional aboriginal (North American) medicines, and
    (B) the medical use of which is based solely on historical and ethnological evidence from references relating to a medical system other than one based on conventional scientific standards.

17-12-97 (2) This Division and Divisions 2 to 4 do not apply to the affixing of a label to a previously labelled container.

C.01A.003. This Division and Divisions 2 to 4 apply to the following distributors:

3-10-02 (a) a distributor of a drug listed in Schedule C or D to the Act or in Schedule F to these Regulations, a controlled drug as defined in subsection G.01.001(1) or a narcotic as defined in the *Narcotic Control Regulations*, who does not hold the drug identification number for the drug or narcotic; and
(b) a distributor of a drug for which that distributor holds the drug identification number.

Prohibition

C.01A.004. (1) Subject to subsection (2), no person shall, except in accordance with an establishment licence,

(a) fabricate, package/label, distribute as set out in section C.01A.003, import or wholesale a drug; or
(b) perform the tests, including examinations, required under Division 2.

19-12-96 (2) A person does not require an establishment licence to perform tests under Division 2 if the person holds an establishment licence as a fabricator, a packager/labeller, a distributor referred to in paragraph C.01A.003(b) or an importer.

3-10-02 (3) No person shall carry on an activity referred to in subsection (1) in respect of a narcotic as defined in the *Narcotic Control Regulations* or a controlled drug as defined in subsection G.01.001(1) unless the person holds a licence for that narcotic or drug under the *Narcotic Control Regulations* or Part G of these Regulations, as the case may be.

Application for Establishment Licence

C.01A.005. Subject to section C.01A.006, a person who wishes to apply for an establishment licence shall submit an application to the Minister, in a form established by the Minister, that contains the following information:

(a) the applicant's name, address and telephone number, and their facsimile number and electronic mail address, if any;
(b) the name and telephone number, and the facsimile number and electronic mail address, if any, of a person to contact in case of an emergency;
(c) each activity set out in Table I to section C.01A.008 for which the licence is requested;
(d) each category of drugs set out in Table II to section C.01A.008 for which the licence is requested;
(e) each dosage form class in respect of which the applicant proposes to carry out a licensed activity, and whether it will be in a sterile dosage form;
19-12-96 (f) whether the applicant proposes to carry out a licensed activity in respect of a drug that is a bulk process intermediate;
(g) the address of each building in Canada in which the applicant proposes to fabricate, package/label, test as required under Division 2 or store drugs, specifying for each building which of those activities and for which category of drugs and, for each category,
  (i) the dosage form classes, and whether any drugs will be in a sterile dosage form, and
  (ii) whether any drugs will be bulk process intermediates;
(h) the address of each building in Canada at which records will be maintained;
(i) whether any building referred to in paragraphs (g) and (h) is a dwelling-house;
(j) the drug identification number, if any, or a name that clearly identifies the drug,
3-10-02 (i) for each narcotic as defined in the *Narcotic Control Regulations* or each controlled drug as defined in subsection G.01.001(1) for which the licence is requested, and
  (ii) for each other drug within a category of drugs for which the licence is requested, unless the licence is to perform tests required under Division 2, distribute as set out in paragraph C.01A.003(a), or wholesale;
(k) if any of the buildings referred to in paragraph (g) have been inspected under the Act or these Regulations, the date of the last inspection;
(l) evidence that the applicant's buildings, equipment and proposed practices and procedures meet the applicable requirements of Divisions 2 to 4;
(m) in the case of an importer of a drug that is fabricated, packaged/labelled or tested in an MRA country at a recognized building,
  (i) the name and address of each fabricator, packager/labeller and tester of the drug and the address of each building at which the drug is fabricated, packaged/labelled or tested, specifying for each building the activities and the category of drug and
    (A) the dosage form class and whether the drug is in a sterile dosage form, and
    (B) whether the drug is a bulk process intermediate,
3-10-02 (ii) in respect of each activity done in an MRA country at a recognized building, the name of the regulatory authority that is designated under subsection C.01A.019(1) in respect of that activity for that drug and that has recognized that building as meeting its good manufacturing practices standards in respect of that activity for that drug, and
  (iii) in respect of any other activities,
    (A) a certificate from a Canadian inspector indicating that the fabricator's, packager/labeller's or tester's buildings, equipment, practices and procedures meet the applicable requirements of Divisions 2 to 4, or
    (B) other evidence establishing that the fabricator's, packager/labeller's or tester's buildings, equipment, practices and procedures meet the applicable reqirements of Divisions 2 to 4;
(n) in the case of any other importer, the name and address of each fabricator, packager/labeller and tester of the drugs proposed to be imported and the address of each building at which the drugs will be fabricated, packaged/labelled and tested, specifying for each building which of those activities and for which category of drugs and, for each category,
  (i) the dosage form classes and whether any drugs will be in a sterile dosage form, and
  (ii) whether any drugs will be bulk process intermediates; and
(o) in the case of an importer referred to in paragraph (n),
  (i) a certificate from a Canadian inspector indicating that the fabricator's, packager/labeller's and tester's buildings, equipment, practices and procedures meet the applicable requirements of Divisions 2 to 4, or
  (ii) other evidence establishing that the fabricator's, packager/labeller's and tester's buildings, equipment, practices and procedures meet the applicable requirements of Divisions 2 to 4.

C.01A.006. (1) A person who wishes to amend an establishment licence shall submit an application to the Minister, in a form established by the Minister, that contains the applicable information specified in section C.01A.005.

(2) An establishment licence must be amended where the licensee proposes

(a) to add an activity or category of drugs, as set out in the tables to section C.01A.008;

(b) in respect of a category of drugs and activity indicated in the licence, to authorize sterile dosage forms of the category;

(c) to add any building in Canada at which drugs are authorized to be fabricated, packaged/labelled, tested as required under Division 2 or stored, or to add, for an existing building, an authorization to fabricate, package/label, test or store a category of drugs, or sterile dosage forms of the category; and

(d) in addition to the matters set out in paragraphs (a) to (c), in the case of an importer,

(i) to add a fabricator, packager/labeller or tester of a drug,

(ii) to amend the name or address of a fabricator, packager/labeller or tester indicated in the licence, and

19-12-96 (iii) if the address of the buildings at which drugs are authorized to be fabricated, packaged/labelled or tested is indicated in the licence, to add additional buildings or, for an existing building, to add an authorization to fabricate, package/label or test a category of drugs, or sterile dosage forms of the category.

C.01A.007. (1) The Minister may, on receipt of an application for an establishment licence or an amended establishment licence, require the submission of further details pertaining to the information contained in the application that are necessary to enable the Minister to process the application.

(2) When considering an application for an establishment licence or an amended establishment licence, the Minister may require that

(a) an inspection be made during normal business hours of any building referred to in paragraph C.01A.005(g) or (h); and

(b) the applicant, if a fabricator, a packager/labeller, a person who performs tests required under Division 2, a distributor referred to in paragraph C.01A.003(b) or an importer, supply samples of any material to be used in the fabrication, packaging/labelling or testing of a drug.

Issuance

C.01A.008. (1) Subject to section C.01A.010, the Minister shall, on receipt of the information and material required by sections C.01A.005 to C.01A.007, issue or amend an establishment licence.

(2) The establishment licence shall indicate

3-10-02 (a) each activity that is authorized and the category of drugs for which each activity is authorized, as set out in the tables to this section, specifying for each activity and category whether sterile dosage forms are authorized;

(b) the address of each building in Canada at which a category of drugs is authorized to be fabricated, packaged/labelled, tested as required under Division 2 or stored, specifying for each building which of those activities and for which category of drugs, and whether sterile dosage forms of the category are authorized; and

(c) in addition to the matters referred to in paragraphs (a) and (b), in the case of an importer,

3-10-02 (i) the name and address of each fabricator, packager/labeller and tester from whom the importer is authorized to obtain the drug for import, and

(ii) the address of each building at which the drug is authorized to be fabricated, packaged/labelled or tested, specifying for each building the activities and the category of drugs that are authorized, and whether sterile dosage forms are authorized.

(3) The Minister may indicate in an establishment licence a period for which records shall be retained under Division 2 that, based on the safety profile of the drug or materials, is sufficient to ensure the health of the consumer.

(4) The Minister may, in addition to the requirements of subsection (2), set out in an establishment licence terms and conditions respecting

(a) the tests to be performed in respect of a drug, and the equipment to be used, to ensure that the drug is not unsafe for use; and
(b) any other matters necessary to prevent injury to the health of consumers, including conditions under which drugs are fabricated, packaged/labelled or tested.

TABLE I

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Item	*Activities*
1.	Fabricate
2.	Package/label
3.	Perform the tests, including any examinations, required under Division 2
4.	Distribute as set out in paragraph C.01A.003(a)
5.	Distribute as set out in paragraph C.01A.003(b)
6.	Import
7.	Wholesale

TABLE II

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Item	*Categories of drugs*
1.	Pharmaceuticals
2.	Vaccines
3.	Whole blood and its components
4.	Drugs listed in Schedule D to the Act, other than vaccines or whole blood and its components
5.	Drugs listed in Schedule C to the Act
6.	Drugs listed in Schedule F to these Regulations, controlled drugs as defined in subsection G.01.001(1) and narcotics as defined in the *Narcotic Control Regulations*

27-6-97 **C.01A.009.** An establishment licence expires on December 31 of each year.

Refusal to Issue

C.01A.010. (1) The Minister may refuse to issue or amend an establishment licence in respect of any or all matters indicated in subsection C.01A.008(2) if

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(a) the applicant has made a false or misleading statement in relation to the application for the licence; or
(b) the applicant has had an establishment licence suspended in respect of the matter.

(2) The Minister shall refuse to issue or amend an establishment licence in respect of any or all matters indicated in subsection C.01A.008(2) if the Minister has reasonable grounds to believe that issuing or amending an establishment licence in respect of the matter would constitute a risk to the health of the consumer.

(3) Where the Minister refuses to issue or amend an establishment licence, the Minister shall

(a) notify the applicant in writing of the reasons for the refusal; and
(b) give the applicant an opportunity to be heard.

Terms and Conditions

23-3-00 **C.01A.011.** (1) Every person who holds an establishment licence shall comply with

19-12-96 (a) the requirements and the terms and conditions of the establishment licence; and
(b) the applicable requirements of Divisions 2 to 4.

23-3-00 (2) Repealed by P.C. 2000-406 of March 23, 2000.

C.01A.012. (1) The Minister may amend the terms and conditions of an establishment licence if the Minister believes on reasonable grounds that an amendment is necessary to prevent injury to the health of the consumer.

(2) The Minister shall give at least 15 days notice in writing to the holder of the establishment licence of the proposed amendment, the reasons for the amendment and its effective date.

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Notification

C.01A.013. Every person who holds an establishment licence shall notify the Minister in writing within 15 days after

(a) there is any change to the information referred to in any of paragraphs C.01A.005(a), (b), (e), (f), (h) and (i), and subparagraphs C.01A.005(g)(i) and (ii); or
(b) an event occurs that results in their being in contravention of any of the applicable requirements of Divisions 2 to 4, where it may affect the quality, safety or efficacy of a drug fabricated, packaged/labelled, tested as required under Division 2 or stored by them.

C.01A.014. (1) No licensee shall carry on a licensed activity in respect of any category of drugs if a change referred to in subsection (2) has occurred in respect of that category, unless

(a) they have filed with the Minister a notice that contains sufficient information to enable the Minister to assess the safety of the drug, taking into account the change; and
19-12-96 (b) the Minister has issued to them a letter indicating that the information will be reviewed and has not, within 90 days after issuing the letter, sent them a notice indicating that the change is not acceptable.

(2) Notification is required in respect of the following changes where they may affect whether a drug can be fabricated, packaged/labelled, tested or stored in accordance with the applicable requirements of Divisions 2 to 4:

(a) changes to the plans and specifications of a building where a drug is fabricated, packaged/labelled, tested or stored;
(b) changes to the equipment that is used in the fabrication, packaging/labelling or testing of a drug;
(c) changes to the practices or procedures; and
3-10-02 (d) in the case of an importer, other than an importer of a drug that is fabricated, packaged/labelled or tested in an MRA country at a recognized building, any change referred to in paragraphs (a) to (c) that relates to the fabricator, packager labeller or tester of the drug being imported.

3-10-02 **C.01A.015.** (1) An importer of a drug that is fabricated, packaged/labelled or tested in an MRA country at a recognized building shall immediately notify the Minister if the fabricator, packager/labeller or tester indicated in the importer's establishment licence no longer holds a valid permit, licence or other authorization issued by the regulatory authority that recognized that building.

(2) The Minister shall, on receiving a notification under subsection (1), amend the importer's establishment licence by removing the name and address of that fabricator, packager/labeller or tester.

Suspension

C.01A.016. (1) Subject to subsection (3), the Minister may suspend an establishment licence in respect of any or all matters indicated in subsection C.01A.008(2) if the Minister has reasonable grounds to believe that

(a) the licensee has contravened any provision of the Act or these Regulations; or
(b) the licensee has made a false or misleading statement in the application for the establishment licence.

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(2) Before suspending an establishment licence, the Minister shall consider

(a) the licensee's history of compliance with the Act and these Regulations; and
(b) the risk that allowing the licence to continue in force would constitute for the health of the consumer.

(3) Subject to subsection C.01A.017(1), the Minister shall not suspend an establishment licence until

(a) an inspector has sent the licensee a written notice that sets out the reason for the proposed suspension, any corrective action required to be taken and the time within which it must be taken;
(b) if corrective action is required, the time set out in the notice has passed without the action having been taken; and
(c) the licensee has been given an opportunity to be heard in respect of the suspension.

C.01A.017. (1) The Minister may suspend an establishment licence without giving the licensee an opportunity to be heard if it is necessary to do so to prevent injury to the health of the consumer, by giving the licensee a notice in writing that states the reason for the suspension.

(2) A licensee may request of the Minister, in writing, that the suspension be reconsidered.

(3) The Minister shall, within 45 days after the date of receiving the request, provide the licensee with the opportunity to be heard.

C.01A.018. The Minister may reinstate an establishment licence after it has been suspended.

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Designation

C.01A.019. (1) For the purposes of this Division and Divisions 2 to 4, a regulatory authority that is set out in column 1 of the table to this section is hereby designated in respect of the activities set out in column 3 for the drug or category of drugs set out in column 2.

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(2) Whole blood and its components are excluded from the drugs and categories of drugs set out in column 2 of the table to this section.

(3) The lot release of drugs listed in Schedule D to the Act is excluded from the activity of testing set out in column 3 of the table to this section.

TABLE

DESIGNATED REGULATORY AUTHORITIES

3-10-02

Item	Column 1 Regulatory authority	Column 2 Drug or category of drugs	Column 3 Activities
1.	Swissmedic, Swiss Agency for Therapeutic Products, Bern, Switzerland	Pharmaceuticals for human or veterinary use Drugs listed in Schedules C and D to the Act	Fabricating, packaging/labelling, testing
2.	Regional Medicines Inspectorate of Northwestern Switzerland (RFS-NW), Basel, Switzerland	Pharmaceuticals for human or veterinary use Drugs listed in Schedules C and D to the Act	Fabricating, packaging/labelling, testing
3.	Regional Medicines Inspectorate of Eastern and Central Switzerland (RFS-OZ), Zurich, Switzerland	Pharmaceuticals for human or veterinary use Drugs listed in Schedules C and D to the Act	Fabricating, packaging/labelling, testing
4.	Regional Medicines Inspectorate of Southern Switzerland (RFS-S), Ticino, Switzerland	Pharmaceuticals for human or veterinary use Drugs listed in Schedules C and D to the Act	Fabricating, packaging/labelling, testing
5.	Regional Medicines Inspectorate of Western Switzerland (RFS-W), Lausanne, Switzerland	Pharmaceuticals for human or veterinary use Drugs listed in Schedules C and D to the Act	Fabricating, packaging/labelling, testing

Good Manufacturing Practices

19-12-96 **C.02.001.** Revoked by P.C. 1996-1915 of December 19, 1996.

C.02.002. In this Division,

19-12-96 "drug" Revoked by P.C. 1996-1915 of December 19, 1996.

"importer" Revoked by P.C. 1996-1915 of December 19, 1996.

7-8-85 "medical gas" means any gas or mixture of gases manufactured, sold or represented for use as a drug; (gaz médical)

"packaging material" includes a label; (matériel d'emballage)

19-12-96 "produce" Revoked by P.C. 1996-1915 of December 19, 1996.

"quality control department" means a quality control department referred to in section C.02.013; (service du contrôle de la qualité)

"specifications" means a detailed description of a drug, the raw material used in a drug or the packaging material for a drug and includes

23-3-89 (a) a statement of all properties and qualities of the drug, raw material or packaging material that are relevant to the manufacture, packaging and use of the drug, including the identity, potency and purity of the drug, raw material or packaging material,

(b) a detailed description of the methods used for testing and examining the drug, raw material or packaging material, and

(c) a statement of tolerances for the properties and qualities of the drug, raw material or packaging material. (spécifications)

Sale

23-3-00 **C.02.003.** No distributor referred to in paragraph C.01A.003(b) and no importer shall sell a drug unless it has been fabricated, packaged/labelled, tested and stored in accordance with the requirements of this Division.

Premises

19-12-96 **C.02.004.** The premises in which a lot or batch of a drug is fabricated or packaged/labelled shall be designed, constructed and maintained in a manner that

(a) permits the operations therein to be performed under clean, sanitary and orderly conditions;

21-5-82 (b) permits the effective cleaning of all surfaces therein; and

(c) prevents the contamination of the drug and the addition of extraneous material to the drug.

Equipment

19-12-96 **C.02.005.** The equipment with which a lot or batch of a drug is fabricated, packaged/labelled or tested shall be designed, constructed, maintained, operated and arranged in a manner that

21-5-82 (a) permits the effective cleaning of its surfaces;

(b) prevents the contamination of the drug and the addition of extraneous material to the drug; and

(c) permits it to function in accordance with its intended use.

Personnel

19-12-96 **C.02.006.** Every lot or batch of a drug shall be fabricated, packaged/labelled, tested and stored under the supervision of personnel who, having regard to the duties and responsibilities involved, have had such technical, academic and other training as the Director considers satisfactory in the interests of the health of the consumer or purchaser.

Sanitation

19-12-96 **C.02.007.** (1) Every person who fabricates or packages/labels a drug shall have a written sanitation program that shall be implemented under the supervision of qualified personnel.

(2) The sanitation program referred to in subsection (1) shall include

19-12-96 (a) cleaning procedures for the premises where the drug is fabricated or packaged/labelled and for the equipment used in the fabrication or packaging/labelling; and

(b) instructions on the sanitary fabrication and packaging/labelling of drugs and the handling of materials used in the fabrication and packaging/labelling of drugs.

19-12-96 **C.02.008.** (1) Every person who fabricates or packages/labels a drug shall have, in writing, minimum requirements for the health and the hygienic behaviour and clothing of personnel to ensure the clean and sanitary fabrication and packaging/labelling of the drug.

19-12-96 (2) No person shall have access to any area where a drug is exposed during its fabrication or packaging/labelling if the person

(a) is affected with or is a carrier of a disease in a communicable form, or

21-5-82 (b) has an open lesion on any exposed surface of the body shall have access to any area where a drug during any stage of its production is exposed.

Raw Material Testing

C.02.009. (1) Each lot or batch of raw material shall be tested against the specifications for the raw material prior to its use in the fabrication of a drug.

(2) No lot or batch of raw material shall be used in the fabrication of a drug unless that lot or batch of raw material complies with the specifications for that raw material.

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(3) Notwithstanding subsection (1), water may, prior to the completion of its tests under that subsection, be used in the fabrication of a drug.

(4) Where any property of a raw material is subject to change on storage, no lot or batch of that raw material shall be used in the fabrication of a drug after its storage unless the raw material is retested after an appropriate interval and complies with its specifications for that property.

(5) Where the specifications referred to in subsections (1), (2) and (4) are not prescribed, they shall

(a) be in writing;

(b) be acceptable to the Director who shall take into account the specifications contained in any publication mentioned in Schedule B to the Act; and

(c) be approved by the person in charge of the quality control department.

C.02.010. (1) The testing referred to in section C.02.009 shall be performed on a sample taken

(a) after receipt of each lot or batch of raw material on the premises of the fabricator; or

19-12-96 (b) subject to subsection (2), before receipt of each lot or batch of raw material on the premises of the fabricator, if

(i) the fabricator

(A) has evidence satisfactory to the Director to demonstrate that raw materials sold to him by the vendor of that lot or batch of raw material are consistently manufactured in accordance with and consistently comply with the specifications for those raw materials, and

21-5-82 (B) undertakes periodic complete confirmatory testing with a frequency satisfactory to the Director, and

(ii) the raw material has not been transported or stored under conditions that may affect its compliance with the specifications for that raw material.

19-12-96 (2) After a lot or batch of raw material is received on the premises of the fabricator, the lot or batch of raw material shall be tested for identity.

Manufacturing Control

C.02.011. (1) Every fabricator, packager/labeller, distributor referred to in paragraph C.01A.003(b) and importer of a drug shall have written procedures prepared by qualified personnel in respect of the drug to ensure that the drug meets the specifications for that drug.

(2) Every person required to have written procedures referred to in subsection (1) shall ensure that each lot or batch of the drug is fabricated, packaged/labelled and tested in compliance with those procedures.

C.02.012. (1) Every fabricator, packager/labeller, distributor referred to in section C.01A.003, importer and wholesaler of a drug shall maintain

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(a) a system of control that permits complete and rapid recall of any lot or batch of the drug that is on the market; and
(b) a program of self-inspection.

(2) Every fabricator and packager/labeller and, subject to subsections (3) and (4), every distributor referred to in paragraph C.01A.003(b) and importer of a drug shall maintain a system designed to ensure that any lot or batch of the drug fabricated and packaged/labelled on premises other than their own is fabricated and packaged/labelled in accordance with the requirements of this Division.

23-3-00 (3) The distributor referred to in paragraph C.01A.003(b) of a drug that is fabricated, packaged/labelled and tested in Canada by a person who holds an establishment licence that authorizes those activities is not required to comply with the requirements of subsection (2) in respect of that drug.

3-10-02 (4) If a drug is fabricated or packaged/labelled in an MRA country at a recognized building, the distributor referred to in paragraph C.01A.003(b) or importer of the drug is not required to comply with the requirements of subsection (2) in respect of that activity for that drug if
(a) the address of the building is set out in that person's establishment licence; and
(b) that person retains a copy of the batch certificate for each lot or batch of the drug received by that person.

Quality Control Department

23-3-00 **C.02.013.** (1) Every fabricator, packager/labeller, distributor referred to in paragraph C.01A.003(b) and importer shall have on their premises in Canada a quality control department that is supervised by personnel described in section C.02.006.

21-5-82 (2) The quality control department referred to in subsection (1) shall be a distinct organizational unit that functions and reports to management independently of any other functional unit, including the manufacturing, processing, packaging or sales unit.

C.02.014. (1) No lot or batch of drug shall be made available for sale unless the sale of that lot or batch is approved by the person in charge of the quality control department.

19-12-96 (2) A drug that is returned to the fabricator, packager/labeller, distributor referred to in paragraph C.01A.003(b) or importer thereof shall not be made available for further sale unless the sale of that drug is approved by the person in charge of the quality control department.

19-12-96 (3) No lot or batch of raw material or of packaging/labelling material shall be used in the fabrication or packaging/labelling of a drug unless the material is approved for that use by the person in charge of the quality control department.

21-5-82 (4) No lot or batch of a drug shall be reprocessed without the approval of the person in charge of the quality control department.

19-12-96 **C.02.015.** (1) All fabrication, packaging/labelling, testing, storage and transportation methods and procedures that may affect the quality of a drug shall be examined and approved by the person in charge of the quality control department before their implementation.

(2) The person in charge of the control department shall cause to be investigated every complaint on quality that is received and cause corrective action to be taken where necessary.

(3) The person in charge of the quality control department shall cause all tests or examinations required pursuant to this Division to be performed by a competent laboratory.

Packaging Material Testing

C.02.016. (1) Each lot or batch of packaging material shall, prior to its use in the packaging of a drug, be examined or tested against the specifications for that packaging material.

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(2) No lot or batch of packaging material shall be used in the packaging of a drug unless the lot or batch of packaging material complies with the specifications for that packaging material.

(3) The specifications referred to in subsections (1) and (2) shall

(a) be in writing;
(b) be acceptable to the Director who shall take into account the specifications contained in any publication mentioned in Schedule B to the Act; and
(c) be approved by the person in charge of the quality control department.

C.02.017. (1) The examination or testing referred to in section C.02.016 shall be performed on a sample taken

(a) after receipt of each lot or batch of packaging material on the premises of the person who packages a drug; or
(b) subject to subsection (2), before receipt of each lot or batch of packaging material on the premises of the person who packages a drug, if
  (i) that person
    (A) has evidence satisfactory to the Director to demonstrate that packaging materials sold to him by the vendor of that lot or batch of packaging material are consistently manufactured in accordance with and consistently comply with the specifications for those packaging materials, and
    (B) undertakes periodic complete confirmatory examination or testing with a frequency satisfactory to the Director,
  (ii) the packaging material has not been transported or stored under conditions that may affect its compliance with the specifications for that packaging material.

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(2) After a lot or batch of packaging material is received on the premises of the person who packages a drug,

(a) the lot or batch of the packaging material shall be examined or tested for identity; and
(b) the labels shall be examined or tested in order to ensure that they comply with the specifications for those labels.

Finished Product Testing

C.02.018. (1) Each lot or batch of a drug shall, prior to its availability for sale, be tested against the specifications for that drug.

(2) No lot or batch of a drug shall be available for sale unless it complies with the specifications for that drug.

(3) The specifications referred to in subsections (1) and (2) shall

(a) be in writing;
(b) be approved by the person in charge of the quality control department; and
(c) comply with the Act and these Regulations.

23-3-00 **C.02.019.** (1) Subject to subsections (3) and (4), in the case of a packager/labeller, distributor referred to in paragraph C.01A.003(b) or importer, the testing referred to in section C.02.018 shall be performed on a sample taken

19-12-96 (a) after receipt of each lot or batch of the drug on the premises in Canada of the packager/labeller, distributor referred to in paragraph C.01A.003(b) or importer of the drug; or

21-5-82 (b) subject to subsection (2), before receipt of each lot or batch of the drug on the premises described in paragraph (a), if

19-12-96 (i) the packager/labeller, distributor referred to in paragraph C.01A.003(b) or importer
  (A) has evidence satisfactory to the Director to demonstrate that drugs sold to him by the vendor of that lot or batch of the drug are consistently manufactured in accordance with and consistently comply with the specifications for those drugs, and

21-5-82 (B) undertakes periodic complete confirmatory testing with a frequency satisfactory to the Director, and

(ii) the drug has not been transported or stored under conditions that may affect its compliance with the specifications for that drug.

19-12-96 (2) Where the packager/labeller, distributor referred to in paragraph C.01A.003(b) or importer of a drug received a lot or batch of the drug on their premises in Canada, and the useful life of the drug is more than 30 days, the lot or batch shall be tested for identity, and the packager/labeller shall confirm the identity after the lot or batch is packaged/labelled.

(3) The distributor referred to in paragraph C.01A.003(b) of a drug that is fabricated, packaged/labelled and tested in Canada by a person who holds an establishment licence that authorizes those activities is not required to comply with the requirements of subsections (1) and (2) in respect of that drug.

3-10-02 (4) If a drug is fabricated, packaged/labelled and tested in an MRA country at a recognized building, the distributor referred to in paragraph C.01A.003(b) or importer of that drug is not required to comply with the requirements of subsections (1) and (2) in respect of that drug if

(a) the address of the building is set out in that person's establishment licence; and
(b) that person retains a copy of the batch certificate for each lot or batch of the drug received by that person.

Records

19-12-96 **C.02.020.** (1) Every fabricator, packager/labeller, distributor referred to in paragraph C.01A.003(b) and importer shall maintain on their premises in Canada, for each drug sold,

(a) master production documents for the drug;
19-12-96 (b) evidence that each lot or batch of the drug has been fabricated, packaged/labelled, tested and stored in accordance with the procedures described in the master production documents;
19-12-96 (c) evidence that the conditions under which the drug was fabricated, packaged/labelled, tested and stored are in compliance with the requirements of this Division;
21-5-82 (d) evidence establishing the period of time during which the drug in the container in which it is sold will meet the specifications for that drug; and
(e) adequate evidence of the testing referred to in section C.02.018.

19-12-96 (2) Every distributor referred to in paragraph C.01A.003(b) and importer shall make available to the Director, on request, the results of testing performed on raw materials and packaging/labelling material for each lot or batch of a drug sold.

19-12-96 (3) Every fabricator shall maintain on his premises

(a) the written specifications for the raw material; and
(b) adequate evidence of the testing of the raw materials referred to in section C.02.009.

21-5-82 (4) Every person who packages a drug shall maintain on his premises

(a) the written specifications for the packaging material; and
(b) adequate evidence of the packaging material examination or testing referred to in section C.02.016.

(5) Every fabricator shall maintain on their premises in Canada

(a) detailed plans and specifications of each building in Canada at which they fabricate, package/label or test; and
19-12-96 (b) a description of the design and construction of those buildings.

(6) Every fabricator, packager/labeller and tester shall maintain on their premises in Canada details of the personnel employed to supervise the fabrication, packaging/labelling and testing, including each person's title, responsibilities, qualifications, experience and training.

C.02.021. (1) Subject to subsection (2), all records and evidence on the fabrication, packaging/labelling, testing and storage of a drug that are required to be maintained under this Division shall be retained for a period of at least one year after the expiration date on the label of the drug, unless otherwise specified in the person's establishment licence.

(2) All records and evidence on the testing of raw materials and packaging/labelling materials that are required to be maintained under this Division shall be retained for a period of at least five years after the materials were last used in the fabrication or packaging/labelling of a drug, unless otherwise specified in the person's establishment licence.

C.02.022. Every distributor referred to in section C.01A.003, wholesaler and importer of a drug shall retain records of the sale of each lot or batch of the drug, which enable them to recall the lot or batch from the market, for a period of at least one year after the expiration date of that lot or batch, unless otherwise specified in their establishment licence.

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C.02.023. (1) On receipt of a complaint respecting the quality of a drug, every distributor referred to in paragraph C.01A.003(b) and importer of the drug shall make a record of the complaint and of its investigation and retain the record for a period of at least one year after the expiration date of the lot or batch of that drug, unless otherwise specified in their establishment licence.

(2) On receipt of any information respecting the quality or hazards of a drug, every distributor referred to in paragraph C.01A.003(b) and importer of the drug shall make a record of the information and retain it for a period of at least one year after the expiration date of the lot or batch of that drug, unless otherwise specified in their establishment licence.

19-12-96 **C.02.024.** (1) Every fabricator, packager/labeller, distributor referred to in section C.01A.003, importer and wholesaler shall

21-5-82 (a) maintain records of the results of the self-inspection program required by section C.02.012 and of any action taken in connection with that program; and
(b) retain those records for a period of at least three years.

19-12-96 (2) Every person who fabricates or packages/labels a drug shall

21-5-82 (a) maintain records on the operation of the sanitation program required to be implemented under section C.02.007; and
(b) retain those records for a period of at least three years.

Samples

C.02.025. (1) Every distributor referred to in paragraph C.01A.003(b) and importer of a drug shall retain in Canada a sample of each lot or batch of the packaged/labelled drug for a period of at least one year after the expiration date on the label of the drug, unless otherwise specified in the distributor's or importer's establishment licence.

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(2) The fabricator shall retain a sample of each lot or batch of raw materials used in the fabrication of a drug for a period of at least two years after the materials were last used in the fabrication of the drug, unless otherwise specified in the fabricator's establishment licence.

21-5-82 **C.02.026.** The samples referred to in section C.02.025 shall be in an amount that is sufficient to determine whether the drug or raw material complies with the specifications for that drug or raw material.

Stability

C.02.027. Every distributor referred to in paragraph C.01A.003(b) and importer shall establish the period of time during which each drug in the package in which it is sold will comply with the specifications.

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C.02.028. Every distributor referred to in paragraph C.01A.003(b) and importer shall monitor, by means of a continuing program, the stability of the drug in the package in which it is sold.

Sterile Products

19-12-96 **C.02.029.** In addition to the other requirements of this Division, a drug that is intended to be sterile shall be fabricated and packaged/labelled

(a) in separate and enclosed areas;
21-5-82 (b) under the supervision of personnel trained in microbiology; and
(c) by a method scientifically proven to ensure sterility.

Medical Gases

7-8-85 **C.02.030.** The provisions of sections C.02.025, C.02.027 and C.02.028 do not apply to medical gases.

Schedule C Drugs

C.03.001. In this DIVISION

(a) "drug" means a drug listed in Schedule C to the Act that is in dosage form, or a drug that is a bulk process intermediate that can be used in the preparation of a drug listed in Schedule C to the Act that is of biological origin; (*drogue*)

19-12-96 (b) Revoked by P.C. 1996-1915 of December 19, 1996.

(c) Revoked by P.C. 1996-1915 of December 19, 1996.

(d) "master lot" means a quantity of a drug from which a lot is prepared for sale by subsequent dilution or mixture,

(e) "radionuclide generator" means a radioactive parent and daughter

(i) contained in an ion exchange column, or

18-12-75 (ii) dissolved in a suitable solvent in a liquid-liquid extraction system where the radioactive daughter is separated from its parent by

(iii) elution from the ion exchange column, or

(iv) a solvent extraction procedure.

19-12-96 **C.03.001.1** No distributor referred to in paragraph C.01A.003(b) or importer shall sell a drug unless it has been fabricated, packaged/labelled, tested and stored in accordance with this Division.

C.03.002. Revoked by P.C. 1996-1915 of December 19, 1996.

C.03.003. Revoked by P.C. 1996-1915 of December 19, 1996.

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C.03.004. Revoked by P.C. 1996-1915 of December 19, 1996.

C.03.005. Revoked by P.C. 1996-1915 of December 19, 1996.

8-1-97 **C.03.006.** to **C.03.011.** are revoked by P.C. 1997-12 of January 8, 1997.

19-12-96 **C.03.012.** On written request from the Director, every fabricator, packager/labeller, tester, distributor referred to in paragraph C.01A.003(b) and importer of a drug shall submit protocols of tests together with samples of any lot or master lot of the drug before it is sold, and no person shall sell a lot of which the protocol or sample fails to meet the requirements of these Regulations.

C.03.013. No person shall fabricate or import a drug that is derived from animal tissue unless the tissue is obtained from a healthy animal free from infectious disease.

C.03.014. (1) Section C.01.004 does not apply to a drug.

(2) Revoked by P.C. 1996-1915 of December 19, 1996.

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(3) Revoked by P.C. 1996-1915 of December 19, 1996.

C.03.015. Every package of a drug listed or described in Schedule F in the Regulations, other than

19-12-96 (a) a drug sold to a drug fabricator,
(b) a drug dispensed pursuant to a prescription,
(c) a radiopharmaceutical as defined in section C.03.201,
or
17-5-01 (d) a component or kit as defined in section C.03.205, shall carry the symbol " **Pr** " on the upper left quarter of the principal display panel of both its inner and outer labels or, in the case of a single dose container, on the upper left quarter of its outer label.

The heading preceding section C.03.030 and sections C.03.030 to C.03.045 are revoked by P.C. 1981-1125 of April 23, 1981.

Sections C.03.050 to C.03.102 (heading "Insulin Preparations") are revoked by P.C. 1982-2379 of August 5, 1982 and renumbered to be C.04.550 to C.04.602 under division 4, heading "Insulin Preparations".

5-8-82 Sections C.03.150 to C.03.156 (heading "Labelling of Insulin Preparations") are revoked by P.C. 1982-2379 of August 5, 1982 and renumbered to be C.04.650 to C.04.656 under division 4, heading "Labelling of Insulin Preparations".

Section C.03.175 to C.03.183 (heading "Anterior Pituitary Extracts" are revoked by P.C. 1982-2379 of August 5, 1982 and renumbered to be C.04.675 to C.04.683 under division 4, heading "Anterior Pituitary Extracts".

Radiopharmaceuticals

19-12-96 **C.03.201.** In these Regulations, "radiopharmaceutical" means a drug that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons.

1-3-79 **C.03.202.** (1) Every package containing a radiopharmaceutical, other than a radionuclide generator, shall carry,

(a) on both the inner and outer labels,

19-12-96 (i) the proper name of the drug, which proper name, where there is a brand name, shall immediately precede or follow the brand name,

(ii) the name of the distributor referred to in paragraph C.01A.003(b), and

20-4-93 (iii) the lot number; and

(b) on the outer label

19-12-96 (i) the address of the distributor referred to in paragraph C.01A.003(b),

(ii) the standard that the drug professes to meet, if that standard is referred to in any publication mentioned in Schedule B to the Act,

(iii) a statement of the pharmaceutical form or the route of administration of the drug,

(iv) a statement of the recommended use and the recommended radioactivity to be administered for that use, or a reference to an accompanying package insert that shows such information,

19-12-96 (v) the establishment licence number of the distributor preceded by the words "Establishment Licence Number", "Numéro de licence d'établissement" or an abbreviation thereof,

(vi) the radiation warning symbol required by the Atomic Energy Control Regulations and the statement "Caution -- Radioactive Material" "Attention -- produits radioactif",

(vii) the names and a statement of the amounts of any preservatives or stabilizing agents contained in the drug,

(viii) the names and a statement of the amounts of all other non-radioactive contents of the drug,

3-9-74 (ix) a statement of the total radioactivity content of the drug including overfill,

(x) a statement of the total volume of the drug including overfill, except where its contents are entirel in gaseous, capsule or lyophilized form,

(xi) a statement of the concentration of radioactive material in the drug expressed as

(A) units of radioactivity per capsule or

(B) units of radioactivity per unit volume,

except where the contents of the drug are entirely in gaseous or lyophilized form,

(xii) a statement of the specific activity of the drug expressed as units of radioactivity per unit weight of carrier present or the statement "carrier-free" or "sans entraineur", whichever is applicable,

(xiii) a statement of the reference time in respect of the radioactivity values mentioned in subparagraphs (ix), (xi) and (xii), the name of the month being written or designated by letter abbreviation,

(xiv) a statement of the recommended useful life or the date after which the drug is not recommended for use, the name of the month being written or designated by letter abbreviation, and

(xv) a statement of the special storage requirements with reference to temperature and light,

7-6-01 (2) Repealed by P.C. 2001-1042 of June 7, 2001.

(3) Subparagraph (1)(b)(viii) does not apply where the information referred to in that subparagraph is shown on a package insert that accompanies the drug.

1-3-79 (4) Section C.01.005 does not apply to a radiopharmaceutical.

1-3-79 **C.03.203.** (1) Every radionuclide generator shall carry on the inner label

19-12-96 (a) the proper name of the radionuclide generator, which proper name, where there is a brand name, shall immediately precede or follow the brand name;
(b) the name and address of the distributor referred to in paragraph C.01A.003(b);
(c) the lot number;
(d) the standard that the radionuclide generator professes to meet, if that standard is referred to in any publication mentioned in Schedule B to the Act;
19-12-96 (e) the establishment licence number of the distributor preceded by the words "Establishment Licence Number", "Numéro de licence d'établissement" or an abbreviation thereof;
(f) the radiation warning symbol required by the Atomic Energy Control Regulations and the statement "Caution -- Radioactive Material" "Attention -- produits radioactif";
(g) a statement of the total parent radioactivity contained in the radionuclide generator;
(h) a statement of the hour and date at which the radioactivity value mentioned in paragraph (g) is valid, the name of the month being written or designated by letter abbreviation;
(i) a statement of the recommended useful life or the date after which the radionuclide generator is not recommended for use, the name of the month being written or designated by letter abbreviation;
(j) a statement of the recommended useful life of the drug after removal from the radionuclide generator;
(k) a statement of special storage requirements with reference to temperature or shielding;
(l) complete directions for use or a reference to an accompanying package insert that sets out such directions; and
18-12-75 (m) a statement cautioning against the dismantling of the radionuclide generator.

(2) Paragraphs (1)(i) and (j) do not apply where the information referred to in those subparagraph is shown on a package insert that accompanies the radionuclide generator.

C.03.204. (1) No person shall sell a drug containing technetium-99m at any time during the useful life of the drug if the drug also contains a radionuclidic impurity mentioned in the monograph for Sodium Pertechnetate Tc-99m Injection referred to in the publication mentioned in item 7 of Schedule B to the Act, in an amount greater than that shown in the monograph.

19-12-96 (2) No person shall sell a radionuclide generator from which can be removed a drug that contains technetium-99m, at any time during the useful life of the drug, if the drug also contains a radionuclidic impurity mentioned in the monograph for Sodium Pertechnetate Tc-99m Injection referred to in the publication mentioned in item 7 of Schedule B to the Act, in an amount greater than that shown in the monograph.

Drugs, other than Radionuclides, Sold or Represented for Use in the Preparation of Radiopharmaceuticals

C.03.205. For the purposes of sections C.03.206 to C.03.209,

"component" means
(a) a unit of a drug, other than a radionuclide, separately packaged in a kit for use in the preparation of a radiopharmaceutical, or
(b) an empty vial or other accessory item in a kit;

"kit" means a package
(a) that contains one or more separately packaged units of a drug, other than a radionuclide, and
(b) that may contain empty vials or other accessory items, for use in the preparation of radiopharmaceuticals.

C.03.206. Section C.01.005 and C.04.019 do not apply to a component or kit.

C.03.207. Every component shall be labelled to show

(a) adequate identification of the component and an adequate description of its function;
(b) where applicable, a quantitative list of its ingredients or a reference to the label of the kit that shows such information;
19-12-96 (c) the name of the distributor referred to in paragraph C.01A.003(b);
(d) the lot number;
(e) a statement of any storage requirements with respect to temperature and light;
(f) the date after which the component is not recommended for use, the name of the month being written in full or designated by letter abbreviation; and
1-3-79 (g) adequate directions for use or a reference to the accompanying package insert that shows such directions.

C.03.208. Every kit shall be labelled to show

(a) its proper name;
20-4-93 (b) its brand name, if any;
(c) a list of its contents;
(d) the name and address of the distributor referred to in paragraph C.01A.003(b);
19-12-96 (e) the establishment licence number of the distributor preceded by the words "Establishment Licence Number", "Numéro de licence d'établissement" or an abbreviation thereof;
(f) the lot number;
(g) a statement of any special storage requirements with respect to temperature and light;
(h) the date after which the kit is not recommended for use, the name of the month being written in full or designated by letter abbreviation;
(i) where the label of a component makes reference to the label of the kit that shows information as to the ingredients of the component, a quantitative list of the ingredients of that component;
(j) a statement of the sterility and a pyrogenicity of the components;
(k) adequate directions for preparing the radiopharmaceutical or a reference to the accompanying package insert that shows such directions;
(l) a statement of the duration of the useful life of the prepared radiopharmaceutical;
(m) a statement of the storage requirements for the prepared radiopharmaceutical;
(n) a statement of the recommended use for the prepared radiopharmaceutical and the recommended radioactivity to be administered for that use, or a reference to the accompanying package insert that shows such information; and
(o) a statement of the route of administration of the prepared radiopharmaceutical.
7-6-01 (p) Repealed by P.C. 2001-1042 of June 7, 2001.

C.03.209. A package insert shall be included in every kit and shall show

20-4-93 (a) the proper name and the brand name, if any, of the kit and a description of its use;
(b) a list of the contents of the kit;
19-12-96 (c) the name and address of the distributor referred to in paragraph C.01A.003(b) of the kit;

(d) identification of the radionuclides that can be used to prepare the radiopharmaceutical;
(e) directions for preparing the radiopharmaceutical and a statement of the storage requirements for the prepared radiopharmaceutical;
(f) a statement of the duration of the useful life of the prepared radiopharmaceutical;
(g) a description of the biological actions of the prepared radiopharmaceutical;
1-3-79 (h) indications and contraindications in respect of the prepared radiopharmaceutical;
(i) warnings and precautions in respect of the components and the prepared radiopharmaceutical;
(j) the adverse reactions, if any, associated with the prepared radiopharmaceutical;
(k) where applicable, the pharmacology and toxicology of the prepared radiopharmaceutical or a statement that such information is available on request;
(l) the radiation dosimetry in respect of the prepared radiopharmaceutical;
(m) a statement of the recommended use for the prepared radiopharmaceutical and the recommended radioactivity to be administered for that use;
(n) a statement of the route of administration of the prepared radiopharmaceutical, and
(o) a recommendation that the radiochemical purity and radioactivity content of the prepared radiopharmaceutical be checked prior to administration.

Schedule D Drugs

C.04.001. In this DIVISION

(a) "date of manufacture" means
  (i) in the case of a product for which a standard of potency exists, the date it satisfactorily passes a potency test,
  (ii) in the case of an animal product for which no standard of potency exists, the date of its removal from the animal, and
  (iii) in the case of a product other than an animal product for which no standard of potency exists, the date of cessation of growth,

19-12-96 (b) "drug" means a drug listed in Schedule D to the Act that is in dosage form, or a drug that is a bulk process intermediate that can be used in the preparation of a drug listed in Schedule D to the Act (drogue).

19-12-96 (c) Revoked by P.C. 1996-1915 of December 19, 1996.

(d) Revoked by P.C. 1996-1915 of December 19, 1996.

C.04.001.1 No distributor referred to in paragraph C.01A.003(b) or importer shall sell a drug unless it has been fabricated, packaged/labelled, tested and stored in accordance with this Division.

C.04.002. This Division does not apply to a drug in oral dosage form that contains micro-organisms if the drug is recommended solely for restoring, normalizing or stabilizing the intestinal flora.

C.04.003. The date of issue of a drug shall be the date on which the finished product is removed for cold storage but in any case shall be, not later than

(a) 6 months after the date of manufacture for a drug that has been kept constantly at a temperature not exceeding 10°C.,
(b) 12 months after the date of manufacture for a drug that has been kept constantly at a temperature not exceeding 5°C., or
(c) two years after the date of manufacture for a drug that has been kept constantly at a temperature not exceeding 0°C.

C.04.004. Revoked by P.C. 1996-1915 of December 19, 1996.
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C.04.005. Revoked by P.C. 1996-1915 of December 19, 1996.

19-12-96 **C.04.006.** Revoked by P.C. 1996-1915 of December 19, 1996.

8-1-97 **C.04.007.** to **C.04.012.** are revoked by P.C. 1997-12 of January 8, 1997.

19-12-96 **C.04.013.** Every fabricator and packager/labeller shall safely segregate all work with spore-bearing, pathogenic microorganisms and other infectious agents known to require special precautions in manipulation and shall take such care of equipment and arrangements for supervision that the possibility of contamination of other drug is avoided.

C.04.014. No person shall conduct laboratory procedures of a diagnostic nature in their premises unless those procedures are entirely segregated from the fabrication, packaging/labelling and testing of drugs.

19-12-96 **C.04.015.** On written request from the Director, every fabricator, packager/labeller, tester, distributor referred to in paragraph C.01A.003(b) and importer of a drug shall submit protocols of tests together with samples of any lot of the drug before it is sold, and no person shall sell any lot of that drug if the protocol or sample fails to meet the requirements of these Regulations.

19-12-96 **C.04.016.** All animals from which drugs are prepared and preserved shall be

(a) under the direct supervision of competent medical or veterinary personnel,
19-12-96 (b) kept in quarantine by the fabricator for at least seven days before use; and
(c) healthy and free from infectious disease.

C.04.017. A fabricator shall keep necropsy records of all animals that die or are killed after having been use in the production of a drug.

19-12-96 **C.04.018.** A fabricator shall immediately segregate, and report the fact to the Minister, any animal with actual or suspected vesicular stomatitis, foot and mouth disease, encephalomyelitis, infectious anaemia, glanders, anthrax, tetanus or any other serious infectious disease.

C.04.019. The provisions of C.01.004 do not apply to a drug as defined in this DIVISION but every package of such drug shall carry

(a) on both the inner and outer labels
19-12-96 (i) the proper name of the drug, which proper name, where there is a brand name, shall immediately precede or follow the brand name in type not less than one-half the size of that of the brand name,
(ii) the name of the distributor referred to in paragraph C.01A.003(b),
(iii) the potency of the drug, where applicable,
(iv) the recommended dose of the drug,
(v) the lot number,
(vi) the expiration date except upon the inner label of a single-dose container, and
(vii) adequate directions for use, and

(b) on the outer label
(i) the address of the distributor referred to in paragraph C.01A.003(b),
19-12-96 (ii) for whole blood and its components, the establishment licence number of the distributor referred to in paragraph C.01A.003(b), preceded by the words "Establishment Licence Number", "Numéro de licence d'établissement" or an abbreviation thereof,
20-4-93 (iii) the proper name, or the common name if there is no proper name, and the amount, of any preservative in the drug,
19-12-96 (iv) a statement that the drug shall be stored at a temperature of not less than 2°C and not more than 10°C, unless the Minister has received evidence demonstrating that such a statement is not required, and
(v) a statement of the net contents in terms of weight, measure, or number.

17-5-01 **C.04.020.** Except in the case of the following drugs, every package of a drug listed in Schedule F of these Regulations shall carry the symbol " Pr " on the upper left quarter of the principal display panel of both its inner and outer labels or, in the case of a single dose container, on the upper left quarter of its outer label:

19-12-96 (a) a drug sold to a person who holds an establishment licence; and

(b) a drug dispensed pursuant to a prescription.

Bacterial Vaccines, Products Anologous to Bacterial Vaccines

C.04.050. Except as provided in this Division, a bacterial vaccine shall be a sterile suspension of killed cultures of bacteria, with or without the addition of other medication, and shall not include an autogenous vaccine.

C.04.051. No person shall sell a bacterial vaccine unless the culture that has been used in its preparation has been tested by an acceptable method for identity and purity and when so tested it shall be true to name and a pure strain, and a record of the culture shall be maintained which shall include a statement of its origin, properties and characteristics.

C.04.052. No fabricator shall use a substrate (culture medium), in the production of a bacterial vaccine, that contains any horse meat or horse serum.

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C.04.053. A fabricator of bacterial vaccine prepared from a bacterium that does not grow readily in ordinary culture media shall test its sterility in media which are specially favourable to the growth of such bacterium, and it shall be sterile.

18-9-58 **C.04.054.** Except as provided in C.04.083, C.04.084 and C.04.090, both the inner and outer labels of every multiple-dose container and the outer label of every single-dose container of a bacterial vaccine shall carry a statement of

(a) the number of bacteria per millilitre, or the weight of dried substance of bacteria per millilitre,

(b) the number of bacteria per millilitre, or the weight of dried substance of bacteria per millilitre, of each species or immunogenic type for a vaccine that contains a number of different species or immunogenic types of bacteria,

(c) the exact nature and amount of any substance, other than a simple diluent, combined with such vaccine and

(d) the recommended dose,

and the inner label of a single-dose container shall carry a statement that it contains only one dose.

C.04.055. The expiration date of a bacterial vaccine shall be not later than 18 months after the date of manufacture or the date of issue.

Typhoid Vaccine

C.04.060. Cultures of Salmonella typhosa used in the preparation of typhoid vaccine shall be smooth, motile and in the Vi form, with the following antigenic structure IX, XII, Vi;d.-.

C.04.061. No person shall sell any lot of typhoid vaccine unless such lot has been shown to meet a test for potency made by an acceptable method.

Pertussis Vaccine

19-12-96 **C.04.065.** A fabricator shall, in the preparation of pertussis (whooping cough) vaccine, use only strains of Bordetella pertussis that meet the requirements of an antigenic test made by an acceptable method.

18-9-58 **C.04.066.** No person shall sell any lot of pertussis (whooping cough) vaccine unless such lot has been shown to meet a test for potency made by an acceptable method.

B.C.G. (Bacille Calmette-Guerin) Vaccine

18-9-58 **C.04.070.** B.C.G. vaccine shall be prepared from living B.C.G. organisms that

(a) have been obtained directly from a source approved by the Director,
(b) are proved to be non-pathogenic by an acceptable method, and
(c) have a history of successful use in the production of B.C.G. vaccine.

19-12-96 **C.04.071.** No fabricator shall employ any person in the manufacture of B.C.G. vaccine unless such person

(a) has been and remains free from all forms of tuberculous infection,
(b) undergoes every 6 months a medical examination, that shall include an X-ray examination of the chest, for the presence of tuberculosis, such examination being made by a qualified, practising physician who shall sign a certificate of such person's freedom from tuberculosis, and such certificate shall be kept on file and be available at all times, and
(c) resides in a household that is at all times free from active tuberculosis,

nor shall a manufacturer employ such person in any other laboratory position.

19-12-96 **C.04.072.** The preparation, preservation and packaging/labelling of B.C.G. vaccine shall be conducted unde the direct supervision of an experienced bacteriologist who has

(a) not less than three years postgraduate training in bacteriology and immunology,
(b) specialized in the field of bacteriology, and
(c) at least one year of practical experience in the manufacture of B.C.G. vaccine.

19-12-96 **C.04.073.** No fabricator shall permit any culture that is not a B.C.G. culture to be at any time on any premises that are used for the manufacture of B.C.G. vaccine.

19-12-96 **C.04.074.** A packager/labeller shall test by an acceptable method, after filling of the final container, each lot of B.C.G. vaccine for the presence of contaminating micro-organisms and when so tested it shall be free there-from.

C.04.075. Notwithstanding C.04.074 a fluid B.C.G. vaccine may be released for sale if no growth has appeared upon the test culture medium after an incubation of 24 hours, but if there is evidence of the presence of contaminating micro-organisms in any lot during the test period of 10 days the packager/labeller shall at once recall such lot.

19-12-96 **C.04.076.** Every fabricator and packager/labeller shall determine the number of viable B.C.G. organisms in each lot of vaccine by an acceptable method and shall keep a record of the number.

19-12-96 **C.04.077.** A fabricator of B.C.G. vaccine shall keep, at a temperature not exceeding 5.0°C, and for not less than 6 months,

(a) the culture on glycerine-water potato medium from which the Sauton I and Sauton II subcultures were made, and
(b) not less than six vials of the final product

from each lot thereof.

19-12-96 **C.04.078.** Every fabricator and packager/labeller of B.C.G. vaccine shall keep, in form satisfactory to the Minister, continuous clinical records of the use of B.C.G. vaccine in humans.

19-12-96 **C.04.079.** A fabricator of B.C.G. vaccine shall examine pathologically all test animals used and shall immediately report to the Minister any evidence of active, progressive tuberculosis in any such animals.

C.04.080. The expiration date for B.C.G. vaccine shall be not more than

(a) ten days after harvesting in the case of fluid vaccine,
11-7-63 (b) twelve months after harvesting in the case of freeze dried vaccine stored at a temperature of 4°C or above, or
(c) twenty months after harvesting in the case of freeze dried vaccine stored at a temperature below 4°C.

C.04.081. No person shall sell fluid B.C.G. vaccine that is not packaged in containers sealed by fusion.

18-9-58 **C.04.082.** No inner label shall be required for fluid B.C.G. vaccine in single-dose containers.

C.04.083. The label of fluid B.C.G. vaccine shall carry, in lieu of the statements provided in C.04.054 (a) and (b), a statement of

18-9-58 (a) the weight of bacteria per millilitre, and

(b) the route of administration of the vaccine.

C.04.084. The label of freeze-dried B.C.G. vaccine shall carry, in lieu of the statements provided in C.04.054 (a) and (b), a statement of

18-9-58 (a) the amount of bacteria per vial or per dose, and

(b) the route of administration of the vaccine.

18-9-58 **C.04.085.** The provisions of C.04.019 (b)(iv) do not apply to freeze-dried B.C.G. vaccine.

Products Analogous to Bacterial Vaccines

C.04.090. A product analogous to a bacterial vaccine shall be

(a) a bacterial antigen, other than a bacterial vaccine, such as a lysate, or

(b) an extract prepared from a bacterial culture,

and shall conform to the requirements of these regulations for bacterial vaccines except those of paragraphs (a) and (b) of C.04.054.

C.04.091. The expiration date of a product analogous to a bacterial vaccine shall be not later than 18 months after the date of manufacture or the date of issue, but for dried tuberculin and tuberculin containing at least 50 per cent glycerin the expiration date shall be not later than five years after the date of manufacture or the date of issue, and for all other tuberculins not more than 12 months after the date of manufacture or the date of issue.

Virus and Rickettsial Vaccines

C.04.100. A virus vaccine, rickettsial vaccine, shall be a suspension of, or prepared from, living or killed viruses or rickettsiae.

19-12-96 **C.04.101.** No person shall sell a virus or a rickettsial vaccine unless the fabricator has submitted to the Minister details of the source of the strains of viruses or rickettsiae used, the method of their propagation, the method of fabrication of the vaccine, the methods employed for determining sterility, safety, identity and potency and any other tests required by these Regulations.

19-12-96 **C.04.102.** Upon written request from the Director every fabricator and packager/labeller shall submit with respect to each lot of virus or rickettsial vaccine, when ready for sale, detailed protocols of sterility, safety, identity, potency, and of any other tests required by these regulations.

Smallpox Vaccine

C.04.110. Smallpox vaccine

(a) shall be a virus vaccine;

(b) shall be the living virus of vaccinia obtained from

(i) the vesicles produced in the skin of healthy calves by inoculation of vaccinia virus,

(ii) specifically infected membranes of chick embryos, or

29-12-66 (iii) suitable tissue culture infected with vaccinia virus; and

(c) may be in fluid or dried form.

19-12-96 **C.04.111.** Every fabricator and packager/labeller shall fabricate and package/label smallpox vaccine only in an independent unit that is isolated from all other laboratory activities, and in or about which no extraneous materials are permitted or stored.

19-12-96 **C.04.112.** A fabricator shall exclude the personnel who care for the vaccine animals from horse stables and paddocks and from contact with horses while smallpox vaccine is being propagated.

C.04.113. Every fabricator and packager/labeller shall dispense smallpox vaccine only in sterile glass containers that are sealed under aseptic conditions.

19-12-96 **C.04.114.** Every fabricator and packager/labeller shall test smallpox vaccine to establish that it is free from

(a) spore-forming anaerobic micro-organisms;

29-12-66 (b) coagulase positive staphylococci;

(c) haemolytic streptococci; and

(d) any other contaminating pathogenic micro-organisms.

C.04.115. Smallpox vaccine, when tested by acceptable methods,

29-12-66 (a) shall be free from extraneous micro-organisms, in the case of vaccine prepared for use by jet gun; and

(b) shall contain not more than 500 viable non-pathogenic bacteria per millilitre, in the case of vaccine prepared for use by the multiple pressure technique or by scarification.

23-11-67 **C.04.116.** Smallpox vaccine, when inoculated in 0.1 ml. amounts of a 1:1,000,000 dilution onto the choriallantois of 10 chick embryos shall produce at least 10 discrete lesions on each membrane.

19-12-96 **C.04.117.** No person shall sell smallpox vaccine unless

(a) in the case of fluid vaccine, it has been stored at a temperature below -10°C;

29-12-66 (b) in the case of dried vaccine, it has been stored at a temperature below 10°C; and

(c) the outer label carries a statement that it shall be stored at a temperature of not more than 5°C.

C.04.118. Notwithstanding the provisions of section C.04.003 the date of issue of smallpox vaccine shall be not later than

23-11-67 (a) in the case of fluid vaccine, 9 months after the date of manufacture; and

(b) in the case of dried vaccine, 24 months after the date of manufacture.

C.04.119. The expiration date of smallpox vaccine shall be not more than

23-11-67 (a) in the case of fluid vaccine, 3 months after the date of issue; and

(b) in the case of dried vaccine, 12 months after the date of issue.

29-12-66 **C.04.120.** No inner label shall be required for smallpox vaccine in single-dose containers or when dispensed in capillary tubes.

29-12-66 **C.04.121.** No person shall sell smallpox vaccine to which an antibiotic has been added.

Poliomyelitis Vaccine

18-9-58 **C.04.122.** Poliomyelitis vaccine shall be an aqueous suspension of killed poliomyelitis viruses, Types I, II and III.

18-9-58 **C.04.123.** Poliomyelitis vaccine shall be prepared in acceptable tissue culture medium from strains of poliomyelitis virus proven capable of producing vaccine of acceptable potency.

18-9-58 **C.04.124.** Poliomyelitis vaccine in its final form shall contain not more than 0.35 milligram per millilitre of total nitrogen, nor more than 1 part per million of animal serum.

18-9-58 **C.04.125.** No person shall sell poliomyelitis vaccine unless it has been tested by an acceptable method for potency and safety and when so tested it shall be safe and of acceptable potency.

18-9-58 **C.04.126.** The outer label shall carry a statement of any antibiotic present in the vaccine.

24-7-85 **C.04.127.** The expiration date of the poliomyelitis vaccine shall be not later than 12 months after the date of the last satisfactory potency test unless evidence, satisfactory to the Director, is presented that a longer period is appropriate.

Poliovirus Vaccine, Live, Oral

C.04.128. **Poliovirus Vaccine, Live, Oral** or **Poliovirus Vaccine, Live, Oral (Naming the strains)** shall be prepared from living poliomyelitis virus types I, II and III that

(a) have been obtained directly from a source acceptable to the Director,
11-7-63 (b) are shown to be genetically stable by an acceptable method,
(c) are shown to be non-pathogenic when given orally to humans,
(d) are proved to be capable of multiplying in the human alimentary tract and of producing type specific neutralizing antibodies when administered orally, and
(e) have a history of successful use in the production of polio virus vaccine, live, oral.

19-12-96 **C.04.129.** Poliovirus vaccine, live, oral, shall be fabricated, packaged/labelled and tested in premises separated from buildings where other products are fabricated, packaged.labelled or tested, and from buildings where control tests involving the use of cell lines or virus strains not employed in the fabrication, packaging/labelling and testing of poliovirus vaccine, live, oral, are carried out.

19-12-96 **C.04.130.** No fabricator shall permit the introduction of any bacterial or viral cultures other than those used in the manufacture of poliovirus vaccine, live, oral on any premises that are used for the manufacture of poliovirus vaccine, live, oral.

19-12-96 **C.04.131.** Notwithstanding sections C.04.129 and C.04.130, a fabricator may manufacture other drugs in an area in which poliovirus vaccine, live, oral is manufactured at times when that vaccine is not being manufactured, if
11-7-63 (a) both prior to and following each manufacture the area is cleaned and disinfected by methods acceptable to the Director, and
(b) the manufacturer has received written permission from the Director to carry out such manufacture.

C.04.132. Poliovirus vaccine, live, oral shall be prepared only
(a) in a tissue culture,
11-7-63 (b) in a medium, and
(c) by methods
acceptable to the Director.

19-12-96 **C.04.133.** No fabricator shall sell poliovirus vaccine, live, oral, unless he has tested each lot for extraneous micro-organisms and the vaccine is free therefrom.

19-12-96 **C.04.134.** A fabricator of poliovirus vaccine, live, oral shall test, by a method acceptable to the Director, each lot of vaccine for neurovirulence and for genetic markers and it shall meet the requirements established by the Director.

19-12-96 **C.04.135.** No fabricator shall employ any person in the manufacture of poliovirus vaccine, live, oral unless such person

11-7-63 (a) is free from infectious disease,
(b) has been vaccinated successfully against poliomyelitis by poliovirus vaccine, live, oral, and
(c) has been proved by periodic tests to be a non-carrier of poliomyelitis virus.

19-12-96 **C.04.136.** A fabricator of poliovirus vaccine, live, oral shall not permit the entry to a building in which the vaccine is manufactured of any person who

11-7-63 (a) is not directly concerned with the manufacturing processes, or
(b) has been working on the same day with experimental animals or with infectious agents.

Bacteriophage

11-7-63 **C.04.137.** Bacteriophage shall be a virus preparation with specific lytic action against microorganisms actually or potentially pathogenic.

11-7-63 **C.04.138.** The expiration date of bacteriophage shall be not later than 12 months after the date of manufacture or the date of issue.

Toxins, Toxoids

Schick Test Reagents

C.04.140. Schick test reagents for the diagnosis of susceptibility to diphtheria shall be

(a) diphtheria toxin for Schick test,
(b) Schick control, and
(c) diphtheria toxin for Schick test with control.

C.04.141. Diphtheria toxin for Schick test shall be sterile diluted diphtheria toxin stabilized by an acceptable method.

C.04.142. Schick control shall be suitably diluted

(a) diphtheria toxoid, or
(b) sterile diphtheria toxin heated at a temperature of 95°C for 5 minutes.

C.04.143. The human test dose of diphtheria toxin for Schick test, when aged toxin containing a preservativ is used, shall be determined by

(a) intracutaneous injection into normal guinea pigs in mixture with different proportions of diphtheria antitoxin, and one test dose mixed with 1/750 or more of a unit of antitoxin must cause no local reactio but mixed with 1/1250 or less of a unit of antitoxin must cause a definite local reaction of the type known as the "positive Schick reaction", and
(b) intracutaneous injection into normal guinea pigs without admixture with antitoxin, and 1/50 of one test dose must not cause, and 1/25 of one test dose must cause, a definite local reaction of the type known as the "positive Schick reaction".

C.04.144. The human test dose of diphtheria toxin for Schick test, when fresh toxin containing no preservative is used, shall be determined by

(a) intracutaneous injection into normal guinea pigs in mixtures with different proportions of diphtheria antitoxin, and one test dose mixed with 1/750 or more of a unit of antitoxin must cause no local reaction, but mixed with 1/1500 or less of a unit of antitoxin must cause a definite local reaction of the type known as the "positive Schick reaction", and
(b) intracutaneous injection into normal guinea pigs without admixture with antitoxin, and 1/100 of one test dose must not cause, and 1/50 of one test dose must cause, a definite local reaction of the type known as the "positive Schick reaction".

C.04.145. The human test dose for the Schick control shall give a negative Schick reaction when injected intracutaneously into normal guinea pigs.

C.04.146. No person shall sell diphtheria toxin for Schick test unless both the inner and the outer labels carry a statement of the number of human test doses it contains together with the name of any stabilizer.

C.04.147. The expiration date of Schick test reagents for the diagnosis of susceptibility to diphtheria shall be not later than 12 months after the date of manufacture or the date of issue.

Diphtheria Toxoid

C.04.160. Liquid diphtheria toxoid shall be sterile, formalized, detoxified diphtheria toxin and shall not contain more than 0.02 per cent free formaldehyde.

C.04.161. Diphtheria toxoid alum precipitated shall be prepared from diphtheria toxoid, and shall not contain more than 15 milligrams of alum per human dose.

C.04.162. The alum used in the preparation of diphtheria toxoid alum precipitated shall contain not less than 99.5 per cent pure potassium alum, A1 K(SO4)2, 12H2O.

19-12-96 **C.04.163.** No fabricator shall use a culture medium for the production of diphtheria toxin that contains horse protein or Witte peptone or that has not been freed as far as possible from any other allergenic ingredient.

C.04.164. Diphtheria toxin from which diphtheria toxoid is prepared shall have a toxicity, as indicated by an L+ dose, of not more than 0.20 millilitre or by an M.L.D. of not more than 0.0025 millilitre.

19-12-96 **C.04.165.** A fabricator shall test each bulk container of diphtheria toxoid, before being dispensed into the final containers, for toxicity by an acceptable method, and it shall be non-toxic.

C.04.166. No person shall sell any lot of diphtheria toxoid unless such lot has been shown to meet a test for antigenicity made by an acceptable method.

19-12-96 **C.04.167.** A fabricator shall fill diphtheria toxoid aseptically into clear glass containers and where preservative is not added shall seal the containers by fusion.

C.04.168. No person shall sell diphtheria toxoid that contains phenol.

C.04.169. No person shall sell diphtheria toxoid unless both the inner and outer labels carry a statement of the appropriate dose for purposes of immunization.

C.04.170. The expiration date of diphtheria toxoid shall be not later than two years after the date of manufacture or the date of issue.

Tetanus Toxoid

C.04.180. Liquid tetanus toxoid shall be sterile, formalized, detoxified tetanus toxin, and shall not contain more than 0.02 per cent free formaldehyde.

C.04.181. Tetanus toxoid alum precipitated shall be prepared from tetanus toxoid, and shall not contain more than 15 milligrams of alum per human dose.

C.04.182. The alum used in the preparation of tetanus toxoid alum precipitated shall contain not less than 99.5 per cent pure potassium alum, Al K(SO4)2, 12H2O.

19-12-96 **C.04.183.** No fabricator shall use a culture medium for the production of tetanus toxin that contains horse protein or Witte peptone or that has not been freed as far as possible from any other allergenic ingredient.

C.04.184. Tetanus toxin from which tetanus toxoid is prepared shall have a toxicity as indicated by an M.L.D. for the guinea pig of not more than 0.0001 millilitre.

19-12-96 **C.04.185.** A packager/labeller shall test each bulk container of tetanus toxoid, before being dispensed into the final containers, for toxicity by an acceptable method, and it shall be non-toxic.

C.04.186. No person shall sell any lot of tetanus toxoid unless such lot has been shown to meet a test for antigenicity made by an acceptable method.

C.04.187. No person shall sell tetanus toxoid unless both the inner and outer labels carry a statement of appropriate dose for purposes of immunization.

19-12-96 **C.04.188.** A fabricator shall fill tetanus toxoid aseptically into clear glass containers and where a preservativ is not added shall seal the container by fusion.

C.04.189. No person shall sell tetanus toxoid that contains phenol.

C.04.190. The expiration date of tetanus toxoid shall be not later than two years after the date of manufacture or the date of issue.

Antitoxins, Antisera

C.04.210. An antitoxin or antiserum shall be the serum or fraction thereof separated from the blood of animals that have been artificially immunized against the by-products or antigenic fractions of specific cultures of micro-organisms, or against specific venoms.

C.04.211. The potency of an antitoxin or antiserum shall be determined by an acceptable method and where applicable the unit of potency shall be the International Unit.

C.04.212. Liquid diphtheria antitoxin shall have a potency of not less than 500 International Units per millilitre.

C.04.213. Liquid tetanus antitoxin shall have a potency of not less than 400 International Units per millilitre.

C.04.214. A liquid antitoxin or antiserum shall contain not more than 20 per cent solids.

C.04.215. A dried antitoxin shall be prepared from a liquid antitoxin and, when reconstituted to the original volume of the liquid antitoxin, shall have a potency not less than that prescribed for such liquid antitoxin.

C.04.216. A dried antitoxin or antiserum shall not contain more than 1 per cent moisture as determined by an acceptable method.

C.04.217. Each lot of antitoxin or antiserum shall be tested by an acceptable method for pyrogenicity and it shall be pyrogen-free, and, after filling into the final containers for identity, and it shall be true to name.

C.04.218. No person shall sell an antitoxin or antiserum unless both the inner and the outer labels carry a statement of the species of animal used, when other than the horse, and the net contents in millilitres or the number of units in the container.

C.04.219. In respect of antitoxins, the expiration date shall be

(a) for liquid antitoxins with standards of potency, not later than 5 years after the date of manufacture,
(b) for dried antitoxins with standards of potency, not later than 5 years after the date of manufacture,
(c) for liquid antitoxins with no standards of potency, not later than 12 months after the date of manufacture,
15-5-68 (d) for dried antitoxins with no standards of potency, not later than 5 years after the date of manufacture.

C.04.220. In respect of antisera, the expiration date shall be

(a) for liquid antisera with standards of potency, not later than 3 years after the date of manufacture,
(b) for dried antisera with standards of potency, not later than 5 years after the date of manufacture,
(c) for liquid antisera with no standards of potency, not later than 12 months after the date of manufacture,
(d) for dried antisera with no standards of potency, not later than 5 years after the date of manufacture.

Preparations from Human Sources

C.04.230. Preparations from human sources shall be pooled blood plasma, or pooled blood serum, or fractions of either separated by a method satisfactory to the Minister.

C.04.231. A fabricator shall obtain human serum, or human plasma, only from a person certified by a qualified medical practitioner to be healthy.

C.04.232. A fabricator shall not use a person to serve as a donor of blood, placenta, or cord who has a history of a disease transmissible by blood transfusion including syphilis, infectious hepatitis or malaria.
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C.04.233. The operation of drawing blood from a donor shall be under the supervision of a qualified medical practitioner, and shall be carried out in a suitable bleeding room under the control of the fabricator.

C.04.234. A fabricator shall obtain human placenta and cord used in the manufacture of preparations from human sources only from women confined in public hospitals, and the donor of such placenta and cord shall have been free from the toxaemias of pregnancy, and the placenta and cord shall not show gross evidence of any pathological condition.

23-4-81 **C.04.235.** (1) Subject to subsections (2) and (3), dried human serum, dried human plasma or dried fraction of either shall not contain more than one per cent moisture when determined by an acceptable method.

(2) Dried RHo(D) Immune Human globulin shall not contain more than 3 per cent moisture when determined by an acceptable method.

(3) Dried Antihemophilic Factor Human shall not contain more than 2 per cent moisture when determined by an acceptable method.

C.04.236. A fabricator shall provide directions or means for the removal of particles of such size as to be dangerous to the recipient from preparations from human sources that are issued in fluid form or that are reconstituted from the dried form.

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C.04.237. A fabricator of preparations from human sources shall maintain complete records of all donors, which records shall include the medical certificate required by C.04.231.

19-12-96 **C.04.238.** A fabricator, packager/labeller or distributor referred to in paragraph C.01A.003(b) may issue human serum or human plasma, or fractions of either of them, for prophylactic or therapeutic use in any of the following forms:

(a) immune human serum, which shall be serum separated from the blood of persons recovered from the disease or from persons specifically immunized against the disease, for which the serum is intended as a prophylactic or therapeutic agent,
(b) immune human globulins, or other immune human serum fractions, which shall be prepared from immune human serum or plasma,
(c) normal human serum, or normal human plasma, or fractions of either of these prepared from the blood of normal individuals, and
(d) dried products prepared from any of these.

C.04.239. No person shall sell a preparation from human sources unless both the inner and the outer labels clearly indicate that the preparation is derived from human sources.

C.04.240. The expiration date for preparations from human sources issued in fluid or dried form shall be not later than 5 years after the date of filling the immediate container.

C.04.300 and **C.04.301** are revoked by P.C. 1981-1125 of April 23, 1981.

Interpretation

24-10-86 **C.04.400.** In this section and sections C.04.401 to C.04.428,

"donor" means a donor of blood for plasmapheresis;

"human plasma" means the fluid portion of blood that has been collected by plasmapheresis and stabilized against clotting;

"plasmapheresis" means the process comprising

(a) the withdrawal of blood from a donor,

(b) the separation of the plasma from the red blood cells, and

(c) the return of the red blood cells to the donor;

22-6-78 "practitioner" means a person registered and licensed under the laws of a province to practise the profession of medicine;

"red blood cell suspension" means red blood cells suspended in sodium chloride solution that have been collected by plasmapheresis and stabilized against clotting.

Application

C.04.401. Sections C.04.402 to C.04.428 do not apply to plasmapheresis performed

(a) for the therapy of a donor;

(b) for the procurement of blood constituents for use in only one recipient;

24-10-85 (c) for medical research; or

(d) for the production of blood grouping sera by a hospital for use within the hospital.

Prohibition

19-12-96 **C.04.402.** No person shall sell or fabricate human plasma or red blood cell suspension except in accordance with sections C.04.403 to C.04.428.

Specific Immunization

C.04.403. (1) Every practitioner shall, before commencing the specific immunization of a donor for the purposes of plasmapheresis,

(a) select the antigen to be injected;

(b) schedule injections of the antigen; and

(c) inform the donor of

22-6-78 (i) the nature of the material to be injected,

(ii) the maximum number of injections to be made,

(iii) the approximate duration of the immunization program, and

(iv) the possible hazards involved.

(2) During the course of every specific immunization program, the practitioner shall

(a) evaluate the donor's clinical response to the program; and

(b) inject the antigen himself or supervise the injection of the antigen by qualified personnel.

Donor Suitability

C.04.404. (1) Every practitioner shall, within 30 days before carrying out on a donor a procedure in a plasmapheresis program involving collection of plasma at intervals of eight weeks or less,

(a) determine the suitability of the donor for plasmapheresis by means of

(i) the review of the donor's medical history, and

(ii) such tests and physical examination as the practitioner deems necessary; and

24-10-85 (b) if the practitioner has determined pursuant to paragraph (a) that the donor is suitable for plasmapheresis, sign a certificate to that effect.

(2) Subsection (1) does not apply where a practitioner has, in respect of the donor, signed a certificate referred to in paragraph (1)(b) within the 12 month period preceding the date on which the procedure is to be carried out.

Plasmapheresis

C.04.405. Every practitioner shall, before commencing a plasmapheresis program, inform the donor of the hazards of the program including the risks of a haemolytic reaction.

C.04.406. (1) A donor who has been provided with a signed certificate pursuant to section C.04.404 shall, on the day that plasmapheresis is to be carried out on him, be interviewed and evaluated by a practitioner or, under the supervision of a practitioner, by a person trained for such a purpose, to ensure that the donor is in good health and, without restricting the generality of such interview and evaluation, to ensure that the donor:

(a) has not donated whole blood within the previous eight weeks;
(b) has a normal temperature;
(c) is free from
  (i) infection, including any infectious skin disease at the site of phlebotomy, and
  (ii) any disease generalized to such an extent as to create a risk of contamination of the human plasma;

(d) is free from any disease transmissible by blood transfusion;
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(e) is free from skin punctures or scars on the arms and forearms indicative of drug addiction;
(f) has a blood pressure within normal limits;
(g) has a
  (i) blood hemoglobin level of not less than 125 grams per litre of blood if the donor is female or 135 grams per litre of blood if the donor is male, or
  (ii) a hematocrit value of 0.38 litre/litre of blood if the donor is female or 0.41 litre/litre if the donor is male;

(h) has a total serum protein of not less than 60 grams per litre of serum;
(i) weighs at least 40 kilograms;
(j) has no history of viral hepatitis;
(k) has not, within the last six months, been in close contact with an individual suffering from viral hepatitis; and
(l) has not, within the last six months, received human blood or any derivative of human blood that is a possible source of viral hepatitis, except for specific immunization performed in accordance with section C.04.403.

(2) Notwithstanding paragraph (1)(a), a donor may donate plasma within eight weeks of a previous donation of whole blood, provided he is examined by a practitioner and that practitioner certifies that the donor otherwise meets the criteria in subsection (1) and that the donor may donate plasma.

C.04.407. Any donor who appears to be under the influence of any drug or alcohol or who for any reason does not appear to be providing reliable answers to questions shall not be considered a suitable donor.

Presence of Practitioner

C.04.408. Plasmapheresis shall be performed only during times that a practitioner, who is fully informed about the plasmapheresis procedure, is present on the premises or can attend the donor within ten minutes of the time the need arises.

Prevention of Contamination

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C.04.409. (1) The skin of a donor at the site of phlebotomy shall be prepared thoroughly and carefully by a method that gives maximum assurance of a sterile container of blood.

(2) The blood of the donor shall be collected, the human plasma shall be separated and the red blood cell suspension shall be returned to the donor by aseptic methods in a sterile collection system.

(3) All surfaces that come in contact with blood or human plasma shall be both sterile and pyrogen-free.

(4) Equipment and waste materials contaminated with blood or human plasma shall be removed immediately following usage for incineration or disinfection.

(5) Any spillage of blood or human plasma shall be treated as a potential source of infection and the area shall be decontaminated immediately.

Samples

24-10-85 **C.04.410.** (1) A sample of blood shall be drawn from each donor within the seven day period prior to the donor's first plasmapheresis in a plasmapheresis program and not less frequently than every three months thereafte for so long as the donor continues on the program

(a) by a practitioner; or

(b) under the supervision of a practitioner, by a person trained for that purpose.

24-10-85 (2) Every sample drawn pursuant to subsection (1) shall be tested by

(a) a laboratory test for syphilis; and

26-4-95 (b) a serum protein electrophoresis test, a quantitative immunodiffusion test, or another test made by an acceptable method to determine the serum protein components.

(3) Within fourteen days after a sample is drawn pursuant to subsection (1), results of the tests specified in subsection (2) shall be reviewed by a practitioner.

24-10-85 (4) Where the test referred to in paragraph (2)(a) is reactive for syphilis, plasmapheresis shall not be carried out again on the donor until the donor's serum proves nonreactive to a laboratory test for syphilis.

(5) Where the test referred to in paragraph (2)(b) shows the plasma protein composition of a dono not to be within normal limits, the donor shall be removed from the plasmapheresis program until those values return to normal.

Review

C.04.411. At least every three months during every plasmapheresis program, all laboratory data and collection records shall be reviewed by a practitioner to determine the continuing suitability of the donor to remain on the program and the practitioner shall sign the review.

C.04.412. Any donor who is, at any time, found not suitable to remain on a plasmapheresis program shall forthwith be removed from the program.

Identification System

19-12-96 **C.04.413.** (1) Every fabricator of human plasma shall establish a donor identification system that positively identifies each donor and relates the records and laboratory data of each donor directly to the donor's blood and its components.

(2) The identification system referred to in subsection (1) shall include the use of a photograph to confirm the donor's identity or some other method that provides equal assurance of positively identifying the donor.

24-10-85 **C.04.414.** Each container of blood and human plasma shall be marked or identified by a number or symbol so as to relate it directly to the donor.

Anticoagulant Solution

C.04.415. A pyrogen-free anticoagulant solution shall be used in every plasmapheresis program consisting o one of the following formulae:

(a) anticoagulant acid citrate dextrose solution (ACD)

Trisodium citrate (Na3C6H5O7.2H2O)	22.0 g
Citric acid (C6H8O7.H2O)	8.0 g
Dextrose (C6H12O6H2O)	24.5 g
Water for Injection (U.S.P.) to make	1 000.0 mL

(b) anticoagulant citrate phosphate dextrose solution (CPD)

Trisodium citrate (Na3C6H5O7.2H2O)	26.3 g
Citric acid (C6H8O7.H2O)	3.3 g
Dextrose (C6H12O6H2O)	25.5 g
Monobasic sodium phosphate (NaH2PO4H2O)	2.2 g
Water for Injection (U.S.P.) to make	1 000.0 mL

24-10-85 (c) Anticoagulant citrate phosphate dextrose adenine solution (CPDA-I)

Trisodium citrate (Na3C6H5O7.2H2O)	26.3 g
Citric acid (C6H8O7.H2O)	3.3 g
Dextrose (C6H12O6H2O)	31.9 g
Monobasic sodium phosphate (NaH2PO4H2O)	2.2 g
Adenine (C5H5N5)	275.0 mg
Water for Injection (U.S.P.) to make	1 000.0 mL

(d) Anticoagulant sodium citrate solution (SC)

Trisodium citrate (Na3C6H5O7.2H2O)	40.0 g
Water for Injection (U.S.P.) to make	1 000.0 mL

Limitations on Plasmapheresis

C.04.416. (1) The maximum quantity of whole blood that may be collected by plasmapheresis from a donor at one time is

(a) where the donor's weight is 40 kg or more but not more than 50 kg, 9 mL per kg of body weight;

24-10-85 (b) where the donor's weight is more than 50 kg but not more than 80 kg, 500 mL;

(c) where the donor's weight is more than 80 kg, 600 mL.

(2) The maximum feasible volume of red blood cell suspension shall be returned to a donor before another unit of whole blood is collected from him.

(3) If the red blood cell suspension of the first collection of whole blood cannot be returned to the donor, then no further collection of blood shall be made for three months.

(4) No more than two donations of plasma shall be collected from a donor within any 48 hour period.

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(5) No more than four donations of plasma shall be collected from a donor within any seven day period.

(6) The maximum quantity of whole blood, not including anticoagulant, that may be collected by plasmapheresis from a donor within any six month period is

(a) where the donor's weight is less than 50 kg, 19 L;

24-10-85 (b) where the donor's weight is 50 kg or more but not more than 80 kg, 26 L;

(c) where the donor's weight is more than 80 kg, 31 L.

Collection

22-6-78 **C.04.417.** (1) All blood for human plasma shall be collected from a donor

(a) by a practitioner; or

(b) under the supervision of a practitioner, by a person trained in the procedure of blood collection.

(2) The human plasma shall, immediately after each blood collection, be separated from the red blood cells.

24-10-85 (3) Sodium chloride for injection, when used to return red blood cell suspension to a donor, shall be obtained from a previously unused container.

General Requirements

Test for Hepatitis B Antigen

C.04.418. Each unit of human plasma shall be nonreactive to a test for the hepatitis B antigen as determined by an acceptable method.

Processing

24-10-85 **C.04.419.** Notwithstanding section C.04.406(j), (k) and (l) and section C.04.418, plasmapheresis may be conducted on a donor whose plasma is reactive to hepatitis B surface antigen or anti-hepatitis B surface antigen to obtain plasma for production of hepatitis B vaccine, hepatitis B immune globulin or for in vitro diagnostic reagents if specific written authorization for such activity has been provided by the Minister.

Containers

19-12-96 **C.04.420.** (1) Containers used for human plasma, whether integrally attached or separated from the original blood container, shall not be entered by the fabricator for any purpose except for filling with human plasma.

(2) Containers used for human plasma shall be uncoloured and hermetically sealed and shall permit clear visibility of the contents.

(3) Containers and their components used for human plasma shall not interact with the plasma under normal conditions of storage and use so as to alter the safety, quality, purity or potency of the plasma and shall provide adequate protection against external factors that may cause deterioration or contamination.

(4) Containers used for human plasma shall, before being filled, be marked or identified by a number or some other symbol that will relate it directly to the donor.

24-10-85 (5) Containers used for human plasma collected from a donor referred to in section C.04.419 shall, after being filled, be handled, stored and packaged separately from other containers.

C.04.421. Human plasma shall not contain a preservative.

C.04.422. No container of human plasma shall contain more than one collection of human plasma.

C.04.423. Any container that is filled with human plasma shall be stored forthwith at -20°C or colder unless the human plasma is intended for the manufacture of reagents.

C.04.424. Human plasma that is frozen shall be inspected at the time of sale and, if there is any evidence of thawing, the unit shall not be sold.

C.04.425. If pilot samples of human plasma are provided, they shall meet the following standards:

(a) prior to filling, all containers of pilot samples shall be marked or labelled so as to relate them directly to the donor of that unit of plasma;
(b) all containers of pilot samples shall be filled at the time the final product is prepared by the person who prepares the final product;
(c) all pilot samples shall be representative of the contents of the final product; and
(d) all pilot samples shall be collected in a manner that does not contaminate the contents of the container.

C.04.426. (1) The labelling provisions of sections C.01.004 and C.04.019 do not apply to human plasma or pilot samples thereof.

22-6-78 (2) In addition to complying with section C.04.414, each container of human plasma, other than a container of a pilot sample, shall be labelled with the following information:

(a) the proper name of the product;

19-12-96 (b) the name, address and establishment licence number of the distributor referred to in paragraph C.01A.003(b);

(c) the donor number or symbol;

(d) the collection date of the plasma;

24-10-85 (e) revoked by P.C. 1985-3195 of October 24, 1985;

(f) the statement: "Store at -20°C or colder" or the appropriate storage temperature where the plasma is intended for the manufacture of reagents;

(g) a statement as to whether the plasma was collected from normal donors or from donors specifically immunized;

(h) the immunizing antigen, if applicable;

(i) the total volume or weight of plasma;

(j) the total quantity and type of anticoagulant used in the plasmapheresis procedure; and

(k) the test for hepatitis B antigen used and the results thereof.

24-10-85 (3) The label of each container used for human plasma that is collected pursuant to section C.04.419 shall bear conspicuous statements that the product may transmit viral hepatitis and that it is to be used for manufacturing purposes only.

19-12-96 **C.04.427.** Revoked by P.C. 1996-1915 of December 19, 1996.

Records

19-12-96 **C.04.428.** (1) In addition to the general record keeping requirements of this Division, every fabricator of human plasma shall keep for each donor

(a) a record of the specific immunization program carried out for the purposes of plasmapheresis, where applicable; and

(b) a complete record of

24-10-85 (i) all examinations, evaluations and reviews required by sections C.04.404, C.04.406, C.04.407, and C.04.411,

(ii) all tests carried out, and

(iii) all interviews conducted.

(2) Each donor record shall be cross-referenced to the units of human plasma associated with the donor.

Insulin Preparations

5-8-82 **C.04.550.** (1) "Insulin" means the active principle of the pancreas that affects the metabolism of carbohydrates in the animal body and that is of value in the treatment of diabetes mellitus.

(2) The Canadian Reference Standard for insulin shall be the International Standard therefor.

(3) The insulin preparations described in these Regulations shall contain insulin to which may be added only such ingredients as are prescribed in these Regulations.

(4) The potency of an insulin preparation shall be expressed in units per cubic centimetre and each unit per cubic centimetre shall provide one International Unit of insulin per cubic centimetre.

5-8-82 **C.04.551.** No person shall sell or dispense an insulin preparation that has not been stored by him continuously at a temperature between 35° and 50°F (2° and 10°C).

5-8-82 **C.04.552.** The zinc-insulin crystals used in an insulin preparation shall contain, as determined by an acceptable method,

(a) not less than 21 International Units of insulin per milligram, and
(b) on the dry basis, not less than 0.30 per cent and not more than 0.90 per cent zinc.

Insulin Injection or Insulin

24-7-85 **C.04.553.** The insulin preparation, "Insulin injection" or "Insulin" shall be a clear colourless or almost colourless sterile solution free from turbidity and insoluble matter, prepared from insulin or zinc insulin crystals, shall have a pH of not less than 2.5 or more than 3.5, or not less than 7.0 or more than 7.8 and shall contain

(a) weight by volume,
  (i) not less than 0.1 per cent and not more than 0.25 per cent of either phenol or cresol, and
  (ii) not less than 1.4 per cent and not more than 1.8 per cent glycerin; and

(b) as determined by an acceptable method, for each 1,000 International Units of insulin,
  (i) not more than 7.0 milligrams of nitrogen for Insulin Injection prepared from zinc-insulin crystals, and not more than 8.5 milligrams of nitrogen for Insulin Injection other than that made from zinc-insulin crystals,
  (ii) not less than 0.10 milligram and not more than 0.40 milligram of zinc for Insulin Injection prepared from zinc-insulin crystals, and not more than 0.40 milligram of zinc for Insulin Injection other than that made from zinc-insulin crystals, and
  (iii) in the case of Insulin Injection other than that made from zinc-insulin crystals, not more than 1.0 milligram of ash.

5-8-82 **C.04.554.** No person shall sell Insulin Injection unless,

(a) it is dispensed in a vial of approximately 10 cubic centimetre capacity that contains an excess volume sufficient to permit withdrawal of 10 cubic centimetres;
(b) the vial label indicates that each cubic centimetre has a potency equal to
  (i) 40 International Units of insulin,
  (ii) 80 International Units of insulin, or
  (iii) 100 International Units of insulin; and
(c) each cubic centimetre thereof has an actual potency that is at least 95 per cent and does not exceed 105 per cent of the potency indicated on the label as determined by an acceptable method.

19-12-96 **C.04.555.** (1) A fabricator shall not sell Insulin Injection unless he

5-8-82 (a) has filed with the Director, in accordance with subsection (2), a submission relating to that preparation, in a form and having a content satisfactory to the Director;
(b) has furnished the Director with such additional information as the Director may require; and
26-4-95 (c) has received from the Director a notice that the information contained in the submission is in accordance with the requirements of this section.

(2) A submission filed pursuant to subsection (1) shall include at least,

(a) for each master lot of insulin or zinc-insulin crystals employed in the manufacture of Insulin Injection
(i) protocols of assay of its potency expressed in International Units per cubic centimetre, in the case of insulin, and in International Units per milligram, in the case of zinc-insulin crystals,
5-8-82 (ii) a report of its moisture content in percentage determined by drying to constant weight at 100°C in the case of zinc-insulin crystals,
(iii) a report of the ash content in the case of insulin, and
(iv) reports of assay of its nitrogen content in milligrams and its zinc content in milligrams per 1,000 International Units of insulin;
(b) for the first finished lot of Insulin Injection prepared from each master lot of insulin or zinc-insulin crystals, a report on the amount of each component thereof; and
(c) for the first filling of the first finished lot of Insulin Injection from each master lot of insulin or zinc-insulin crystals,
26-4-95 (i) a report of assay of its nitrogen content in milligrams per 1,000 International Units of insulin,
(ii) a report of assay of its zinc content in milligrams per 1,000 International Units of insulin, and
(iii) a report on the determination of its pH.

19-12-96 **C.04.556.** The expiration date printed on the inner and outer labels of every package of Insulin Injection shal be a date not later than two years after the date of removal for distribution from the fabricator's place of storage.

Insulin Zinc Suspension -- Rapid

24-7-85 **C.04.557.** The insulin preparation "Insulin Zinc Suspension--Rapid" shall be a sterile suspension in a buffered aqueous medium, of insulin modified by the addition of zinc in such a way that the suspended precipitate consists of amorphous material, shall have a pH of not less than 7.0 and not more than 7.8 and shall contain

(a) weight by volume,
(i) not less than 0.15 per cent and not more than 0.17 per cent of sodium acetate (NaC2H3O 23H2O),
(ii) not less than 0.65 per cent and not more than 0.75 per cent of sodium chloride, and
(iii) not less than 0.09 per cent and not more than 0.11 per cent of methyl-p-hydroxybenzoate; and

(b) as determined by an acceptable method, for each 1,000 International Units of insulin,
10-7-80 (i) not more than 7.0 milligrams of nitrogen; and
(ii) not less than 1.2 milligrams and not more than 2.5 milligrams of zinc, of which not less than 20 per cent and not more than 65 per cent shall be in the supernatant liquid.

5-8-82 **C.04.558.** The insulin used in the preparation of Insulin Zinc Suspension--Rapid shall be obtained from one or more master lots and shall be present in an amount sufficient to provide either 40, 80 or 100 International Units of insulin in each cubic centimetre of Insulin Zinc Suspension--Rapid when the precipitate is suspended uniformly.

5-8-82 **C.04.559.** The clear supernatant liquid obtained from Insulin Zinc Suspension--Rapid shall contain not more than 1.0 International Unit of insulin per cubic centimetre when the potency of the insulin preparation is 40 units per cubic centimetre, and not more than 1.5 International Units of insulin per cubic centimetre when the potency of the insulin preparation is either 80 units or 100 units per cubic centimetre, as determined by an acceptable method.

5-8-82 **C.04.560.** No person shall sell Insulin Zinc Suspension--Rapid unless

(a) it is dispensed in a vial of approximately 10 cubic centimetre capacity that contains an excess volume sufficient to permit withdrawal of 10 cubic centimetres; and
(b) each cubic centimetre thereof provides, when the precipitate is suspended uniformly,
(i) 40 International Units of insulin,
(ii) 80 International Units of insulin, or
8-1-74 (iii) 100 International Units of insulin.

19-12-96 **C.04.561.** (1) A fabricator shall not sell Insulin Zinc Suspension--Rapid unless he

(a) has filed with the Director, in accordance with subsection (2), a submission relating to that preparation, in a form and having a content satisfactory to the Director;
(b) has furnished the Director such additional information as the Director may require; and
26-4-95 (c) has received from the Director a notice that the information contained in the submission is in accordance with the requirements of this section.

(2) A submission filed pursuant to subsection (1) shall include at least,

(a) for each master lot of insulin or zinc-insulin crystals employed in the manufacture of Insulin Zinc Suspension--Rapid,
(i) protocols of assay of its potency expressed in International Units per cubic centimetre in the case of insulin, and in International Units per milligram in the case of zinc-insulin crystals,
(ii) a report of its moisture content in percentage determined by drying to constant weight at 100°C in the case of zinc-insulin crystals, and
5-8-82 (iii) reports of assay of its nitrogen content in milligram and its zinc content in milligrams per 1,000 International Units of insulin;

(b) for the first finished lot of Insulin Zinc Suspension--Rapid prepared from each master lot of insulin or zinc-insulin crystals
(i) a report on the amount of each component used in the preparation,
(ii) a report of assay of its nitrogen content per 1,000 International Units of insulin,
(iii) a report of assay of its zinc content per 1,000 International Units of insulin,
(iv) a report of the insulin content in International Units per cubic centimetre of the supernatant liquid after removal of the suspended precipitate,
(v) a report of assay of the zinc content of the supernatant liquid after removal of the suspended precipitate,
(vi) a report on the determination of its pH, and
(vii) a report on the microscopic appearance of the suspended precipitate; and

(c) for the first filling of the first finished lot of Insulin Zinc Suspension--Rapid from each master lot of insulin or zinc-insulin crystals,
26-4-95 (i) a report on the determination of its pH,
(ii) a report on the microscopic examination of the precipitate, and
(iii) a report on its identification, as determined by an acceptable method.

5-8-82 **C.04.562.** The expiration date printed on the inner and outer labels of every package of Insulin Zinc Suspension--Rapid shall be a date not later than two years after the date of filling of the immediate container.

Insulin Zinc Suspension -- Medium

24-7-85 **C.04.563.** The insulin preparation "Insulin Zinc Suspension--Medium" shall be a sterile suspension, in a buffered aqueous medium, of insulin modified by the addition of zinc in such a way that the suspended precipitate consists of a mixture of crystals and amorphous material in an approximate ratio of seven parts of crystals to three parts of amorphous material, shall have a pH of not less than 7.0 and not more than 7.8 and shall contain

(a) weight by volume,
(i) not less than 0.15 per cent and not more than 0.17 per cent of sodium acetate ($NaC_2H_3O_2 \cdot 3H_2O$),
(ii) not less than 0.65 per cent and not more than 0.75 per cent of sodium chloride, and
(iii) not less than 0.09 per cent and not more than 0.11 per cent of methyl-p-hydroxybenzoate; and

(b) as determined by an acceptable method, for each 1,000 International Units of insulin,
16-6-88 (i) not more than 7.0 milligrams of nitrogen of which not less than 63 per cent and not more than 73 per cent shall be in the crystalline component, and
10-7-80 (ii) not less than 1.2 milligrams and not more than 2.5 milligrams of zinc, of which not less than 20 per cent and not more than 65 per cent shall be in the supernatant liquid.

5-8-82 **C.04.564.** The insulin used in the preparation of Insulin Zinc Suspension--Medium shall be obtained from one or more master lots and shall be present in an amount sufficient to provide either 40, 80 or 100 International Units of insulin in each cubic centimetre of the preparation when the precipitate is suspended uniformly.

5-8-82 **C.04.565.** The clear supernatant liquid obtained from Insulin Zinc Suspension--Medium shall contain not more than 1.0 International Unit of insulin per cubic centimetre when the potency of the insulin preparation is 40 units per cubic centimetre, and not more than 1.5 International Units of insulin per cubic centimetre when the potency of the insulin preparation is either 80 units or 100 units per cubic centimetre, as determined by an acceptable method.

5-8-82 **C.04.566.** No person shall sell Insulin Zinc Suspension--Medium unless

(a) it is dispensed in a vial of approximately 10 cubic centimetre capacity that contains an excess volume sufficient to permit withdrawal of 10 cubic centimetres; and
(b) each cubic centimetre thereof provides, when the precipitate is suspended uniformly,
(i) 40 International Units of insulin,
(ii) 80 International Units of insulin, or
8-1-74 (iii) 100 International Units of insulin.

19-12-96 **C.04.567.** (1) A fabricator shall not sell Insulin Zinc Suspension--Medium unless he

(a) has filed with the Director, in accordance with subsection (2), a submission relating to that preparation, in a form and having a content satisfactory to the Director;
(b) has furnished the Director with such additional information as the Director may require; and
26-4-95 (c) has received from the Director a notice that the information contained in the submission is in accordance with the requirements of this section.

(2) A submission filed pursuant to subsection (1) shall include at least,

(a) for each master lot of insulin or zinc-insulin crystals employed in the manufacture of Insulin Zinc Suspension--Medium,
(i) protocols of assay of its potency expressed in International Units per cubic centimetre in the case of insulin, and in International Units per milligram in the case of zinc-insulin crystals,
(ii) a report of its moisture content in percentage determined by drying to constant weight at 100°C in the case of zinc-insulin crystals, and
(iii) reports of assay of its nitrogen content in milligrams and its zinc content in milligrams per 1,000 International Units of insulin;

5-8-82 (b) for the first finished lot of Insulin Zinc Suspension--Medium prepared from each master lot of insulin or zinc-insulin crystals,
(i) a report on the amount of each component used in the preparation,
(ii) a report of assay of its nitrogen content in milligrams per cubic centimetre or per 1,000 International Units of insulin,
(iii) a report of assay of its zinc content in milligrams per cubic centimetre or per 1,000 International Units of insulin,
(iv) a report of the insulin content, in International Units per cubic centimetre, of the supernatant liquid after removal of the suspended precipitate,
(v) a report on the determination of the proportion of the nitrogen in the crystalline component of the suspended precipitate,
(vi) a report of assay of the zinc content of the supernatant liquid after removal of the suspended precipitate,
(vii) a report on the determination of its pH, and
(viii) a report on the microscopic appearance of the suspended precipitate; and

(c) for the first filling of the first finished lot of Insulin Zinc Suspension--Medium from each master lot of insulin or zinc-insulin crystals,
26-4-95 (i) a report on the determination of its pH,
(ii) a report on the microscopic examination of the precipitate, and
(iii) a report on its identification as determined by an acceptable method.

5-8-82 **C.04.568.** The expiration date printed on the inner and outer labels of Insulin Zinc Suspension--Medium shall be a date not later than two years after the date of filling of the immediate container.

Insulin Zinc Suspension -- Prolonged

24-7-85 **C.04.569.** The insulin preparation "Insulin Zinc Suspension--Prolonged" shall be a sterile suspension in a buffered aqueous medium of insulin modified by the addition of zinc in such a way that the suspended precipitate consists of crystals with not more than a trace of amorphous material, shall have a pH of not less than 7.0 and not more than 7.8 and shall contain

16-2-67 (a) weight by volume,

(i) not less than 0.15 per cent and not more than 0.17 per cent of sodium acetate ($NaC_2H_3O_2 3H_2O$),

(ii) not less than 0.65 per cent and not more than 0.75 per cent of sodium chloride, and

(iii) not less than 0.09 per cent and not more than 0.11 per cent of methyl- **p**-hydroxybenzoate; and

(b) as determined by an acceptable method, for each 1,000 International Units of insulin,

(i) not more than 7.0 milligrams of nitrogen, of which not less than 90 per cent shall be in the crystalline component, and

10-7-80 (ii) not less than 1.2 milligrams and not more than 2.5 milligrams of zinc, of which not less than 20 per cent and not more than 65 per cent shall be in the supernatant liquid.

5-8-82 **C.04.570.** The insulin used in the preparation of Insulin Zinc Suspension--Prolonged shall be obtained from one or more master lots and shall be present in an amount sufficient to provide either 40, 80 or 100 International Units of insulin in each cubic centimetre of the preparation when the precipitate is suspended uniformly.

5-8-82 **C.04.571.** The clear supernatant liquid obtained from Insulin Zinc Suspension--Prolonged shall contain not more than 1.0 International Unit of insulin per cubic centimetre when the potency of the insulin preparation is 40 units per cubic centimetre, and not more than 1.5 International Units of insulin per cubic centimetre when the potency of the insulin preparation is either 80 units or 100 units per cubic centimetre, as determined by an acceptable method.

5-8-82 **C.04.572.** No person shall sell Insulin Zinc Suspension--Prolonged unless

(a) it is dispensed in a vial of approximately 10 cubic centimetre capacity that contains an excess volume sufficient to permit withdrawal of 10 cubic centimetres; and

(b) each cubic centimetre thereof provides, when the precipitate is suspended uniformly,

(i) 40 International Units of insulin,

(ii) 80 International Units of insulin, or

8-1-74 (iii) 100 International Units of insulin.

19-12-96 **C.04.573.** (1) A fabricator shall not sell Insulin Zinc Suspension--Prolonged unless he

(a) has filed with the Director, in accordance with subsection (2), a submission relating to that preparation, in a form and having a content satisfactory to the Director;

(b) has furnished the Director with such additional information as the Director may require; and

26-4-95 (c) has received from the Director a notice that the information contained in the submission is in accordance with the requirements of this section.

(2) A submission filed pursuant to subsection (1) shall include at least,

(a) for each master lot of insulin or zinc-insulin crystals employed in the manufacture of Insulin Zinc Suspension--Prolonged,

(i) protocols of assay of its potency expressed in International Units per cubic centimetre in the case of insulin, and in International Units per milligram in the case of zinc-insulin crystals,

(ii) a report of its moisture content in percentage determined by drying to constant weight at 100°C in the case of zinc-insulin crystals, and

(iii) reports of assay of the nitrogen content in milligrams and of its zinc content in milligrams per 1,000 International Units of insulin;

5-8-82 (b) for the first finished lot of Insulin Zinc Suspension--Prolonged prepared from each master lot of insulin or zinc-insulin crystals,

(i) a report on the amount of each component used in the preparation,

(ii) a report of assay of its nitrogen content in milligrams per cubic centimetre or per 1,000 International Units of insulin,

(iii) a report of assay of its zinc content in milligrams per cubic centimetre or per 1,000 International Units of insulin,

(iv) a report of the insulin content, in International Units per cubic centimetre, of the supernatant liquid after removal of the suspended precipitate,

(v) a report of the determination of the proportion of the nitrogen in the crystalline component of the suspended precipitate,

(vi) a report of assay of the zinc content of the supernatant liquid after removal of the suspended precipitate,

(vii) a report on the determination of its pH, and

(viii) a report on the microscopic appearance of the suspended precipitate; and

(c) for the first filling of the first finished lot of Insulin Zinc Suspension--Prolonged from each master lot of insulin or zinc-insulin crystals,

(i) a report on the determination of its pH,

26-5-95 (ii) a report on the microscopic examination of the precipitate, and

(iii) a report on its identification as determined by an acceptable method.

5-8-82 **C.04.574.** The expiration date printed on the inner and outer labels of every package of Insulin Zinc Suspension--Prolonged shall be a date not later than two years after the date of filling of the immediate container.

Globin Insulin with Zinc

C.04.575. The insulin preparation "**Globin Insulin with Zinc**" shall be a sterile solution of insulin modified by the addition of globin prepared from beef blood, in the form of globin hydrochloride, and zinc, shall be a clear, yellowish, or almost colourless liquid free from insoluble matter and acceptably free from turbidity, shall hav a pH of not less than 3.4 and not more than 3.8 and shall contain,

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(a) weight by volume, not less than 1.3 per cent and not more than 1.7 per cent glycerin, and either

(i) not less than 0.15 per cent and not more than 0.20 per cent cresol, or

(ii) not less than 0.20 per cent and not more than 0.26 per cent phenol, and

(b) as determined by an acceptable method, for each 1,000 International Units of insulin,

(i) not more than 15.0 milligrams of total nitrogen,

(ii) not less than 36.0 milligrams and not more than 40.0 milligrams of globin calculated as 6.0 times the nitrogen content of the globin, and

(iii) not less than 2.5 milligrams and not more than 3.5 milligrams of zinc.

5-8-82 **C.04.576.** The globin hydrochloride used in the preparation of Globin Insulin with Zinc shall contain not less than 16.0 per cent and not more than 17.5 per cent nitrogen calculated on a dry, ash-free and hydrochloric acid-free basis, and its ash content shall be not more than 0.3 per cent as determined by an acceptable method.

5-8-82 **C.04.577.** The insulin used in the preparation of Globin Insulin with Zinc shall be obtained from one or more master lots and shall be present in an amount sufficient to provide either 40 or 80 International Units of insulin in each cubic centimetre of the Globin Insulin with Zinc.

5-8-82 **C.04.578.** (1) The Canadian Reference Standard for Globin Insulin with Zinc shall be the standard adopted therefor by the Director from time to time.

19-12-96 (2) Upon application of a person who holds an establishment licence, the Director shall furnish him with a portion of the Canadian Reference Standard with directions for comparative testing.

(3) The testing of the biological reaction of Globin Insulin with Zinc shall be made by an acceptable method and that biological reaction shall be comparable to the biological reaction of the portion of the Canadian Reference Standard furnished by the Director.

5-8-82 **C.04.579.** No person shall sell Globin Insulin with Zinc unless

(a) it is dispensed in a vial of approximately 10 cubic centimetre capacity that contains an excess volume sufficient to permit withdrawal of 10 cubic centimetres; and

(b) each cubic centimetre thereof provides,

(i) 40 International Units of insulin, or

(ii) 80 International Units of insulin.

19-12-96 **C.04.580.** (1) A fabricator shall not sell Globin Insulin with Zinc unless he

5-8-82 (a) has filed with the Director, in accordance with subsection (2), a submission relating to that preparation, in a form and having a content satisfactory to the Director;

(b) has furnished the Director with such additional information as the Director may require; and

26-4-95 (c) has received from the Director a notice that the information contained in the submission is in accordance with the requirements of this section.

(2) A submission filed pursuant to subsection (1) shall include at least,

(a) for each master lot of insulin or zinc-insulin crystals employed in the manufacture of Globin Insulin with Zinc,
  (i) protocols of assay of its potency expressed in International Units per cubic centimetre in the case of insulin, and in International Units per milligram in the case of zinc-insulin crystals,
  (ii) a report of its moisture content in percentage determined by drying to constant weight at 100°C in the case of zinc-insulin crystals, and
  (iii) reports of assay of its nitrogen content in milligrams and its zinc content in milligrams per 1,000 International Units of insulin;

(b) for the master lot of globin hydrochloride used in the preparation of Globin Insulin with Zinc, reports of assay of
  (i) its nitrogen content in per cent calculated on a dry, ash-free and hydrochloric acid-free basis,
  (ii) its chloride content in per cent calculated as hydrochloride, and
  (iii) its ash content in percentage;

5-8-82 (c) for the components used in the preparation of the trial mixture of Globin Insulin with Zinc, a report on the quantity of
  (i) insulin in grams, or in International Units,
  (ii) zinc in grams, or in milligrams, per 1,000 International Units of insulin,
  (iii) globin hydrochloride in grams or in milligrams, per 1,000 International Units of insulin, and
  (iv) the volume of the preparation in cubic centimetre or litres;

(d) for the trial mixture of Globin Insulin with Zinc,
  (i) a report of assay of its nitrogen content in milligrams per cubic centimetre or per 1,000 International Units of insulin,
  (ii) a report of assay of its zinc content in milligrams per cubic centimetre or per 1,000 International Units of insulin,
  (iii) protocols of the biological reaction showing the retardation of the insulin effect, and
  (iv) a report on the determination of its pH;

(e) for the first finished lot of Globin Insulin with Zinc from each trial mixture of Globin Insulin with Zinc, a report on the amount of each component in the preparation; and

(f) for the first filling of the first finished lot of Globin Insulin with Zinc from each trial mixture of Globin Insulin with Zinc,
  (i) a report of assay of its nitrogen content in milligrams per cubic centimetre or per 1,000 International Units of insulin,

26-4-95 (ii) a report of assay of its zinc content in milligrams per cubic centimetre or per 1,000 International Units of insulin, and
  (iii) a report on the determination of its pH.

5-8-82 **C.04.581.** The expiration date printed on the inner and outer labels of every package of Globin Insulin with Zinc shall be a date not later than two years after the date of filling of the immediate container.

NPH Insulin or Isophane Insulin

24-7-85 **C.04.582.** The insulin preparation "NPH Insulin" or "Isophane Insulin" shall be a sterile preparation of rod-shaped crystals containing insulin, protamine and zinc, suspended in a buffered aqueous medium, shall have a pH of not less than 7.0 and not more than 7.8 and shall contain

(a) weight by volume, not less than 0.15 per cent and not more than 0.25 per cent anhydrous disodium phosphate, and either
  (i) not less than 1.4 per cent and not more than 1.8 per cent glycerin and not less than 0.15 per cent and not more than 0.17 per cent metacresol and not less than 0.06 and not more than 0.07 per cent phenol, or
  (ii) not less than 0.40 per cent and not more than 0.45 per cent sodium chloride and not less than 0. per cent and not more than 0.9 per cent glycerin and not less than 0.18 per cent and not more than 0.22 per cent metacresol; and

(b) as determined by an acceptable method, for each 1,000 International Units of insulin,
  (i) not more than 8.5 milligrams of nitrogen,
  (ii) not less than 3.0 milligrams and not more than 6.0 milligrams of protamine except that the ratio o the protamine to the insulin shall be not less than the isophane ratio and shall not exceed the isophane ratio by more than 10 per cent, and

28-8-74 (iii) not less than 0.10 milligram and not more than 0.40 milligram of zinc, and
8-1-74 (iv) no protease activity significant for the stability of NPH Insulin.

5-8-82 **C.04.583.** The protamine used in preparing NPH Insulin shall be obtained from the sperm or from the mature testes of fish belonging to the family Salmonidae, genera Oncorhynchus Suckley, or Salmo Linne.

5-8-82 **C.04.584.** The "isophane ratio" means the minimum number of milligrams of protamine required to precipitate 100 International Units of insulin and shall be determined by an acceptable method.

5-8-82 **C.04.585.** The insulin used in the preparation of NPH Insulin shall be obtained from one or more master lots and shall be present in an amount sufficient to provide either 40, 80 or 100 International Units of insulin in each cubic centimetre of the preparation when the precipitate is suspended uniformly.

5-8-82 **C.04.586.** The clear supernatant liquid obtained from NPH Insulin shall contain not more than 0.4 International Units of insulin per cubic centimetre when the potency of the insulin preparation is 40 units per cubic centimetre, not more than 0.6 International Units of insulin per cubic centimetre when the potency of the insulin preparation is 80 units per cubic centimetre and not more than 0.7 International Units of insulin per cubic centimetre when the potency of the insulin preparation is 100 units per cubic centimetre, as determined by an acceptable method.

5-8-82 **C.04.587.** No person shall sell NPH Insulin unless

(a) it is dispensed in a vial of approximately 10 cubic centimetre capacity that contains an excess volume sufficient to permit withdrawal of 10 cubic centimetres; and
(b) each cubic centimetre thereof provides,
(i) 40 International Units of insulin,
(ii) 80 International Units of insulin, or
8-1-74 (iii) 100 International Units of insulin.

19-12-96 **C.04.588.** (1) A fabricator shall not sell NPH Insulin unless he
(a) has filed with the Director, in accordance with subsection (2), a submission relating to that preparation, in a form and having a content satisfactory to the Director;
(b) has furnished the Director with such additional information as the Director may require; and
26-4-95 (c) has received from the Director a notice that the information contained in the submission is in accordance with the requirements of this section.

(2) A submission filed pursuant to subsection (1) shall include at least,
(a) for each master lot of zinc-insulin crystals employed in the manufacture of NPH Insulin,
(i) protocols of assay of its potency in International Units per milligram,
(ii) a report of its moisture content in per cent determined by drying to constant weight at 100°C, and
(iii) reports of assay of its nitrogen content in milligrams and its zinc content in milligrams per 1,000 International Units of insulin;
(b) for the master lot of protamine, a report of the isophane ratio for the insulin used in the preparation of the NPH Insulin;
(c) for the trial mixture of NPH Insulin,
(i) a report of assay of its nitrogen content in milligrams per cubic centimetre or per 1,000 International Units of insulin,
5-8-82 (ii) a report of assay of its zinc content in milligrams per cubic centimetre or per 1,000 International Units of insulin,
(iii) a report of the insulin content in International Units per cubic centimetre of the supernatant liquid after removal of the suspended precipitate,
(iv) a report on the determination of its pH, and
(v) a report on the microscopic examination of the precipitate;
(d) for the first finished lot of NPH Insulin from each trial mixture of NPH Insulin, a report on the amount of each component in the preparation; and
(e) for the first filling of the first finished lot of NPH Insulin from each trial mixture of NPH Insulin,
(i) a report of assay of its nitrogen content in milligrams per cubic centimetre or per 1,000 International Units of insulin,
(ii) a report of assay of its zinc content in milligrams per cubic centimetre or per 1,000 International Units of insulin,
(iii) a report on the determination of its pH,
26-4-95 (iv) a report on the microscopic examination of the precipitate, and
(v) a report of its identification as determined by an acceptable method.

5-8-82 **C.04.589.** The expiration date printed on the inner and outer labels of NPH Insulin shall be a date not later than two years after the date of filling of the immediate container.

Protamine Zinc Insulin

5-8-82 **C.04.590.** The insulin preparation "**Protamine Zinc Insulin**" shall be a sterile white suspension in a buffered aqueous medium, containing insulin modified by the addition of protamine and zinc, shall have a pH of not less than 7.1 and not more than 7.4, and shall contain,

(a) weight by volume
  (i) not less than 0.15 per cent and not more than 0.25 per cent anhydrous disodium phosphate,
  (ii) not less than 1.4 per cent and not more than 1.8 per cent glycerin, and
  (iii) either not less than 0.18 per cent and not more than 0.22 per cent cresol, or not less than 0.22 per cent and not more than 0.28 per cent phenol; and

(b) as determined by an acceptable method, for each 1,000 International Units of insulin,
  (i) not more than 12.5 milligrams of total nitrogen,
  (ii) not less than 10.0 milligrams and not more than 15.0 milligrams of protamine, and
16-7-74 (iii) not less than 1.7 milligrams and not more than 2.5 milligrams of zinc.

5-8-82 **C.04.591.** The protamine used in the preparation of Protamine Zinc Insulin shall be obtained from the sperm or from the mature testes of fish belonging to the family Salmonidae, genera Oncorhynchus Suckley or Salmo Linne.

5-8-82 **C.04.592.** The insulin used in the preparation of Protamine Zinc Insulin shall be obtained from one or more master lots and shall be present in an amount sufficient to provide either 40, 80 or 100 International Units of insulin in each cubic centimetre of the preparation when the precipitate is suspended uniformly.

5-8-82 **C.04.593.** (1) The Canadian Reference Standard for Protamine Zinc Insulin shall be the standard adopted therefor by the Director from time to time.

19-12-96 (2) Upon application of a person who holds an establishment licence, the Director shall furnish him with a portion of the Canadian Reference Standard with directions for comparative testing.

(3) The testing of the biological reaction of Protamine Zinc Insulin shall be made by an acceptable method and that biological reaction shall be comparable to the biological reaction of the portion of the Canadian Reference Standard furnished by the Director.

5-8-82 **C.04.594.** No person shall sell Protamine Zinc Insulin unless

(a) it is dispensed in a vial of approximately 10 cubic centimetre capacity that contains an excess volume sufficient to permit withdrawal of 10 cubic centimetres; and

(b) each cubic centimetre thereof provides
  (i) 40 International Units of insulin,
  (ii) 80 International Units of insulin, or
8-1-74 (iii) 100 International Units of insulin.

19-12-96 **C.04.595.** (1) A fabricator shall not sell Protamine Zinc Insulin unless he

5-8-82 (a) has filed with the Director, in accordance with subsection (2), a submission relating to that preparation, in a form and having a content satisfactory to the Director;

(b) has furnished the Director with such additional information as the Director may require; and

26-4-95 (c) has received from the Director a notice that the information contained in the submission is in accordance with the requirements of this section.

(2) A submission filed pursuant to subsection (1) shall include at least,

(a) for each master lot of insulin or zinc-insulin crystals employed in the manufacture of Protamine Zinc Insulin,
5-8-82 (i) protocols of assay of its potency in International Units per cubic centimetre in the case of insulin and in International Units per milligram in the case of zinc-insulin crystals,
  (ii) a report on its moisture content in percentage determined by drying to constant weight at 100°C i the case of zinc-insulin crystals, and
  (iii) reports of assay of its nitrogen content in milligrams, and its zinc content in milligrams per 1,000 International Units of insulin;

(b) for the components used in the preparation of the trial mixture of Protamine Zinc insulin, a report on the quantity of
(i) insulin in grams or in International Units,
(ii) zinc in grams or in milligrams, per 1,000 International Units of insulin,
(iii) protamine in grams or in milligrams, per 1,000 International Units of insulin, and
(iv) the volume of the preparation in cubic centimetres or litres;

(c) for the trial mixture of Protamine Zinc Insulin,
(i) a report of assay of its nitrogen content in milligrams per cubic centimetre or per 1,000 International Units of Insulin,
5-8-82 (ii) a report of assay of its zinc content in milligrams per cubic centimetre or per 1,000 International Units of insulin,
(iii) protocols of its biological reaction showing retardation of the insulin effect, and
(iv) a report on the determination of its pH;
(d) for the first finished lot of Protamine Zinc Insulin from each trail mixture of Protamine Zinc Insulin, a report on the amount of each component in the preparation; and
(e) for the first filling of the first finished lot of Protamine Zinc Insulin from each trial mixture of Protamine Zinc Insulin,
(i) a report of assay of its nitrogen content in milligrams per cubic centimetre or per 1,000 International Units,
26-4-95 (ii) a report of assay of its zinc content in milligrams per cubic centimetre or per 1,000 International Units, and
(iii) a report on the determination of its pH.

5-8-82 **C.04.596.** The expiration date printed on the inner and outer labels of every package of Protamine Zinc Insulin shall be a date not later than two years after the date of filling of the immediate container.

Sulphated Insulin

5-8-82 **C.04.597.** The insulin preparation "**Sulphated Insulin**" shall be a clear or slightly turbid, colourless or almost colourless, sterile, isotonic preparation of zinc-insulin crystals chemically modified by treatment with sulphuric acid, shall have a pH of not less than 6.0 and not more than 7.0, and shall contain,

(a) weight by volume,
(i) not less than 0.6 per cent and not more than 1.0 per cent sodium chloride, and
(ii) not less than 0.2 per cent and not more than 0.3 per cent phenol; and

(b) as determined by an acceptable method,
(i) not more than 200 milligrams protein for each 1,000 International Units of insulin, and
(ii) not less than 5.5 and not more than 6.5 sulphate groups per insulin molecule.

5-8-82 **C.04.598.** The "neutralization ratio" means the amount of anti-beef-insulin serum required to neutralize one unit of Sulphated Insulin divided by the amount required to neutralize one unit of beef insulin, and shall be determined by an acceptable method.

5-8-82 **C.04.599.** The neutralization ratio of Sulphated Insulin shall be not less than 4 to 1.

5-8-82 **C.04.600.** No person shall sell Sulphated Insulin unless

(a) it is dispensed in a vial of approximately 10 cubic centimetre capacity that contains an excess volume sufficient to permit withdrawal of 10 cubic centimetres, and
(b) each cubic centimetre thereof provides 100 International Units of insulin as determined by an acceptable method.

19-12-96 **C.04.601.** (1) A fabricator shall not sell Sulphated Insulin unless he

5-8-82 (a) has filed with the Director, in accordance with subsection (2) a submission relating to that preparation, in a form and having a content satisfactory to the Director;
(b) has furnished the Director with such additional information as the Director may require; and
26-4-95 (c) has received from the Director a notice that the information contained in the submission is in accordance with the requirements of this section.

(2) A submission filed pursuant to subsection (1) shall include at least,

(a) for each master lot of zinc-insulin crystals employed in the manufacture of Sulphated Insulin,

5-8-82 (i) protocols of assay of its potency in International Units per milligram,

(ii) a report of its moisture content in percentage determined by drying to constant weight at 100°C, and

(iii) reports of assay of its nitrogen content in milligrams and its zinc content in milligrams per 1,000 International Units of insulin; and

(b) for each lot of Sulphated Insulin prepared from each master lot of zinc-insulin crystals,

(i) a report of the amount of each component,

(ii) a report of the protein content in milligrams per 1,000 International Units of insulin,

(iii) a report on the determination of the neutralization ratio,

(iv) a report on the determination of the number of sulphate groups per insulin molecule,

26-4-95 (v) protocols of assay of its potency expressed as International Units per cubic centimetre, and

(vi) a report on the determination of its pH.

5-8-82 **C.04.602.** The expiration date printed on the inner and outer labels of every package of Sulphated Insulin shall be a date not later than two years after the date of filling of the immediate container.

Labelling of Insulin Preparations

19-12-96 **C.04.650.** The packager/labeller of Insulin Injection may label that insulin preparation "Insulin made from Zinc-Insulin crystals" only when it has been prepared from zinc-insulin crystals.

19-12-96 **C.04.651.** The packager/labeller of an insulin preparation shall print the information required by these Regulations to appear on both the inner and outer labels of every package of that insulin preparation as set out in the Table to this section.

TABLE

	Item	Column I Insulin Preparation	Column II Potency of Preparation	Column III Special Printing Requirements for Label
8-1-74	1	Insulin Injection, not labelled as set out in item 2.	(a) 40 units per cc. (b) 80 units per cc. (c) 100 units per cc.	(a) black ink on yellow stock. (b) black ink on green stock. (c) black ink on white stock.
8-1-74	2	Insulin Injection, labelled "Insulin made from Zinc-Insulin crystals".	(a) 40 units per cc. (b) 80 units per cc. (c) 100 units per cc.	(a) red ink on grey stock. (b) green ink on grey stock. (c) black ink on white stock.
8-1-74	3	Insulin Zinc Suspension--Rapid, Insulin Zinc Suspension--Medium and Insulin Zinc Suspension--Prolonged.	(a) 40 units per cc. (b) 80 units per cc. (c) 100 units per cc.	(a) red ink on lavender stock plus a distinguishing mark or design. (b) green ink on lavender stock plus a distinguishing mark or design. (c) black ink on white stock.
	4	Globin Insulin with Zinc.	(a) 40 units per cc. (b) 80 units per cc.	(a) red ink on brown stock except that the expression "40 units per cubic centimetre" may be printed in white letters on a red background. (b) green ink on brown stock except that the expression "80 units per cubic centimetre" may be printed in white letters on a green background.
8-1-74	5	NPH Insulin.	(a) 40 units per cc. (b) 80 units per cc. (c) 100 units per cc.	(a) red ink on blue stock. (b) green ink on blue stock. (c) black ink on white stock.
8-1-74	6	Protamine Zinc Insulin.	(a) 40 units per cc. (b) 80 units per cc. (c) 100 units per cc.	(a) red ink on white stock. (b) green ink on white stock. (c) black ink on white stock.
	7	Sulfated Insulin.	(a) 100 units per cc.	(a) black ink on white stock plus the statement "Warning ... Not for Ordinary Use ... See Package Leaflet".

19-12-96 **C.04.652.** The packager/labeller of an insulin preparation shall print on the outer label of every package thereof instructions to store the preparation in a refrigerator at 35° to 50°F (2° to 10°C) and to avoid exposing it to freezing.

19-12-96 **C.04.653.** The packager/labeller of an insulin preparation that consists of a precipitate suspended in a buffered aqueous medium shall print on the inner label of every package thereof the statement "Shake Carefully".

19-12-96 **C.04.654.** The packager/labeller of an insulin preparation may, in lieu of printing adequate directions for its use on both the inner and outer labels thereof as required by subparagraphs C.04.019(a)(vii), print the description for use in a descriptive circular prepared in accordance with section C.04.655, but in such case he shall

(a) enclose a copy of the circular in the package containing the preparation; and
(b) state on the outer label of the package that such a circular is enclosed therein.

5-8-82 **C.04.655.** The descriptive circular referred to in section C.04.654 shall include, at least, the following information:

(a) a statement that
  (i) the treatment of diabetes mellitus requires medical supervision and review,
  (ii) insulin preparations should be used only as determined by a physician for each patient in the ligh of blood-sugar and urinary-sugar findings, and
  (iii) the physician's instructions concerning diet, dosage, rest and exercise should be followed carefully;

(b) an outline of the procedure to be followed in withdrawing the insulin preparation from the vial, including techniques for sterilization of the syringe and needle, vial-stopper and site of injection;
(c) a statement explaining the injections should be subcutaneous, and not intravenous or intramuscular, and a caution against successive injections in any one site;
(d) a statement that doses are specified in terms of Units of potency per cubic centimetre and that the volume of each dose will depend upon the potency in terms of units per cubic centimetre stated on the label of the insulin preparation and that, for these reasons, it is important that the patient understand the marking on syringes;
(e) a brief explanation of hypoglycemia together with emergency measures suitable for use by patients and those caring for patients in the event of hypoglycemic reactions;
(f) a statement indicating the possibility of undesirable reactions associated with illness or infection, with the omission or loss of a meal, and with a shortage of the insulin preparation;
(g) a statement warning against using any other type of insulin preparation than that prescribed by the physician;
(h) a statement that the use of a package should not be commenced after the expiration date printed on the package;
(i) a statement that the contents should be used as continuously as practicable and that any vial from which a part of the contents has been withdrawn should be discarded in the vent of its being in disuse for several weeks' time;
(j) a statement stressing the importance of visiting a physician regularly and of carefully following his instructions;
(k) in the case of insulin preparations consisting of a clear, colourless or almost colourless solution, free from turbidity and from insoluble matter, a statement that if the contents of the vial become cloudy or turbid, use of that vial should be discontinued;
(l) in the case of insulin preparations consisting of a precipitate suspended in a buffered aqueous medium, a statement explaining that it is necessary to shake the vial carefully before withdrawing a dose, noting that if the contents have become lumpy or granular in appearance or have formed a deposit of particles on the wall of the container, the use of that vial should be discontinued;
(m) instructions that the insulin preparation should be stored in a refrigerator at 35°-50°F (2°-10°C) and should not be exposed to freezing; and
(n) in the case of Sulphated Insulin, a statement explaining that this insulin preparation is not for ordinary use, but is a chemically modified insulin which may be more effective than the usual insulin preparations in certain insulin-resistant or insulin-allergic diabetic patients.

19-12-96 **C.04.656.** (1) Notwithstanding section C.04.554, a person who holds an establishment licence may sell Insulin Injection made from zinc-insulin crystals contained in vials of approximately 20 cubic centimetre capacity each of which vials

(a) contains an excess volume sufficient to permit withdrawal of 20 cubic centimetres, and

(b) provides 500 International Units of insulin per cubic centimetre,

if

(c) notwithstanding section C.04.651, both the inner and outer labels are printed in black ink on white stock and overprinted in narrow brown and white diagonal stripes, of which there shall be at least 5 but not more than 20 to each inch,

(d) both the inner and the outer labels carry the statement "Warning--High Potency -- Not for Ordinary Use" and

(e) each package contains a descriptive circular that conforms to the requirements of section C.04.655 and, in addition, includes,

(i) at the beginning of the circular the statement:

5-8-82 "Warning--This insulin preparation contains 500 International Units of insulin in each cubic centimetre. Extreme caution must be observed in the measurement of doses because inadvertent over-dose may result in irreversible shock. Serious consequences may result if it is used other than under constant medical supervision. Unless specifically prescribed it should never be used by patients to replace use of any other insulin preparation.",

(ii) a statement that Insulin made from Zinc-Insulin crystals 500 International Units per cubic centimetre should not be administered intravenously, and

(iii) a statement giving information for the safe and effective use by physicians of the drug in insulin shock therapy and in the treatment of diabetic patients with high insulin resistance (daily requirement more than 200 International Units of insulin).

26-5-95 (2) Revoked by P.C. 1995-664 of April 26, 1995.

Anterior Pituitary Extracts

5-8-82 **C.04.675.** Anterior pituitary extract shall include all natural products, prepared from the anterior lobe of the pituitary gland of animals, having physiological properties associated with the hormones of the anterior pituitary gland and their proper names shall be

(a) **Adrenocorticotrophic Hormone, Corticotrophin,**

(b) **Thyrotrophic Hormone, Thyrotrophin,**

(c) **Growth Hormone Pituitary, Somatotrophin,**

(d) **Lactogenic Hormone, Prolactin,**

(e) **Gonadotrophic Hormone, Gonadotrophin,** following by qualifying words to indicate gonadotrophic activity associated with the extract,

and if unpurified anterior pituitary extract

(f) **Pituitary Extract Anterior Lobe** followed by qualifying words to indicate the physiological properties associated with it.

5-8-82 **C.04.676.** Reference standards for anterior pituitary extract shall be

(a) the International Standard,
(b) where no International Standard exists, the Canadian Reference Standard shall be that established and kept by the Director from whom portions for comparative testing may be had upon application; and
19-12-96 (c) where neither an International Standard nor a Canadian Reference Standard exists, a provisional reference standard that shall be a suitable quantity of the product submitted by the distributor referred to in paragraph C.01A.003(b) to the Director for checking the uniformity of the product.

4-12-97 **C.04.677.** Both the inner and the outer labels of an anterior pituitary extract shall carry a statement of the potency in terms of the reference standard for anterior pituitary extract provided in section C.04.676 as determined by an acceptable method, except that where no reference standard for an anterior pituitary extract exists, the distributor referred to in paragraph C.01A.003(b) shall include, with every package of the anterior pituitary extract, an acceptable statement of the unit of potency and the method of assay used.

19-12-96 **C.04.678.** No person who holds an establishment licence shall sell corticotrophic hormones for subcutaneou or intramuscular use unless the preparation has been assayed by an acceptable method involving subcutaneous injection and, where the preparation is recommended for intravenous use, the label carries specific dosage instructions for the use.

5-8-82 **C.04.679.** No person shall sell as such adrenocorticotrophic hormone, thyrotrophic hormone, growth hormone pituitary, lactogenic hormone, or gonadotrophic hormone that is not acceptably free from any anterior pituitary extract other than the one for which it is named.

20-4-93 **C.04.680.** The outer label of a mixture of two or more of adrenocorticotrophic hormone, thyrotrophic hormone, growth hormone pituitary, lactogenic hormone and gonadotrophic hormone, or a mixture of any of those with pituitary extract anterior lobe, shall carry a declaration of the proper name and the amount of each component of the mixture.

5-8-82 **C.04.681.** The outer label of an anterior pituitary extract or mixture of anterior pituitary extracts shall carry a statement

(a) showing the species of animal from which the glands used in the preparation of the anterior pituitary extract were obtained;
(b) that it shall be stored at refrigerator temperature; and
21-12-61 (c) that, except in the case of gonadotrophic hormones, it is to be used only on the advice or on the prescription of a physician.

5-8-82 **C.04.682.** Both the inner and the outer labels of adrenocorticotrophic hormone shall carry a statement indicating the route of administration, in addition to meeting the requirements of paragraphs C.04.681 (a) and (b).

5-8-82 **C.04.683.** The expiration date for an anterior pituitary extract or mixture of anterior pituitary extracts shall be not more than two years after the date of passing a potency test.

DRUGS FOR CLINICAL TRIALS INVOLVING HUMAN SUBJECTS

Interpretation

C.05.001. The definitions in this section apply in this Division.

"adverse drug reaction" means any noxious and unintended response to a drug that is caused by the administration of any dose of the drug. (*réaction indésirable à une drogue*)

"adverse event" means any adverse occurrence in the health of a clinical trial subject who is administered a drug, that may or may not be caused by the administration of the drug, and includes an adverse drug reaction. (*incident thérapeutique*)

"clinical trial" means an investigation in respect of a drug for use in humans that involves human subjects and that is intended to discover or verify the clinical, pharmacological or pharmacodynamic effects of the drug, identify any adverse events in respect of the drug, study the absorption, distribution, metabolism and excretion of the drug, or ascertain the safety or efficacy of the drug. (*essai clinique*)

"drug" means a drug for human use that is to be tested in a clinical trial. (*drogue*)

"good clinical practices" means generally accepted clinical practices that are designed to ensure the protection of the rights, safety and well-being of clinical trial subjects and other persons, and the good clinical practices referred to in section C.05.010. (*bonnes pratiques cliniques*)

"import" means to import a drug into Canada for the purpose of sale in a clinical trial. (*importer*)

"investigator's brochure" means, in respect of a drug, a document containing the preclinical and clinical data on the drug that are described in paragraph C.05.005(e). (*brochure du chercheur*)

"protocol" means a document that describes the objectives, design, methodology, statistical considerations and organization of a clinical trial. (*protocole*)

"qualified investigator" means the person responsible to the sponsor for the conduct of the clinical trial at a clinical trial site, who is entitled to provide health care under the laws of the province where that clinical trial site is located, and who is

(a) in the case of a clinical trial respecting a drug to be used for dental purposes only, a physician or dentist and a member in good standing of a professional medical or dental association; and

7-6-01 (b) in any other case, a physician and a member in good standing of a professional medical association. (*chercheur qualifié*)

"research ethics board" means a body that is not affiliated with the sponsor, and

(a) the principal mandate of which is to approve the initiation of, and conduct periodic reviews of, biomedical research involving human subjects in order to ensure the protection of their rights, safety and well-being; and

(b) that has at least five members, that has a majority of members who are Canadian citizens or permanent residents under the *Immigration Act*, that is composed of both men and women and that includes at least

(i) two members whose primary experience and expertise are in a scientific discipline, who have broad experience in the methods and areas of research to be approved and one of whom is from a medical discipline or, if the clinical trial is in respect of a drug to be used for dental purposes only, is from a medical or dental discipline,

(ii) one member knowledgeable in ethics,

(iii) one member knowledgeable in Canadian laws relevant to the biomedical research to be approved,

(iv) one member whose primary experience and expertise are in a non-scientific discipline, and

(v) one member who is from the community or is a representative of an organization interested in the areas of research to be approved and who is not affiliated with the sponsor or the site where the clinical trial is to be conducted. (*comité d'éthique de la recherche*)

"serious adverse drug reaction" means an adverse drug reaction that requires in-patient hospitalization or prolongation of existing hospitalization, that causes congenital malformation, that results in persistent or significant disability or incapacity, that is life threatening or that results in death. (*réaction indésirable grave à une drogue*)

"serious unexpected adverse drug reaction" means a serious adverse drug reaction that is not identified in nature, severity or frequency in the risk information set out in the investigator's brochure or on the label of the drug. (*réaction indésirable grave et imprévue à une drogue*)

"sponsor" means an individual, corporate body, institution or organization that conducts a clinical trial. (*promoteur*)

Application

C.05.002. (1) Subject to subsection (2), this Division applies to the sale or importation of drugs to be used for the purposes of clinical trials involving human subjects.

(2) Except for paragraph C.05.003(a), subsections C.05.006(2) and (3), paragraphs C.05.010(a) to (i), section C.05.011, subsections C.05.012(1) and (2), paragraphs C.05.012(3)(a) to (d) and (f) to (h), subsection C.05.012(4) and sections C.05.013, C.05.016 and C.05.017, this Division does not apply to the sale or importation of a drug for the purposes of a clinical trial authorized under subsection C.05.006(2).

Prohibition

C.05.003. Despite sections C.01.014, C.08.002 and C.08.003, no person shall sell or import a drug for the purposes of a clinical trial unless

(a) the person is authorized under this Division;

(b) the person complies with this Division and sections C.01.015, C.01.036, C.01.037 to C.01.040, C.01.040.2, C.01.064 to C.01.067, C.01.070, C.01.131, C.01.133 to C.01.136, and C.01.435; and

(c) if the drug is to be imported, the person has a representative in Canada who is responsible for the sale o the drug.

General

C.05.004. Despite these Regulations, a sponsor may submit an application under this Division to sell or import a drug for the purposes of a clinical trial that contains a substance the sale of which is prohibited by these Regulations, if the sponsor establishes, on the basis of scientific information, that the inclusion of the substance in the drug may result in a therapeutic benefit for a human being.

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Application for Authorization

C.05.005. An application by a sponsor for authorization to sell or import a drug for the purposes of a clinical trial under this Division shall be submitted to the Minister, signed and dated by the sponsor's senior medical or scientific officer in Canada and senior executive officer and shall contain the following information and documents:

(a) a copy of the protocol for the clinical trial;

(b) a copy of the statement, as it will be set out in each informed consent form, that states the risks and anticipated benefits arising to the health of clinical trial subjects as a result of their participation in the clinical trial;

(c) a clinical trial attestation, signed and dated by the sponsor's senior medical or scientific officer in Canada and senior executive officer, containing
  (i) the title of the protocol and the clinical trial number,
  (ii) the brand name, the chemical name or the code for the drug,
  (iii) the therapeutic and pharmacological classifications of the drug,
  (iv) the medicinal ingredients of the drug,
  (v) the non-medicinal ingredients of the drug,
  (vi) the dosage form of the drug,
  (vii) the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the sponsor,
  (viii) if the drug is to be imported, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the sponsor's representative in Canada who is responsible for the sale of the drug,
  (ix) for each clinical trial site, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the qualified investigator, if known at the time of submitting the application,

(x) for each clinical trial site, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the research ethics board that approved the protocol referred to in paragraph (a) and approved an informed consent form containing the statement referred to in paragraph (b), if known at the time of submitting the application, and

(xi) a statement

(A) that the clinical trial will be conducted in accordance with good clinical practices and these Regulations, and

(B) that all information contained in, or referenced by, the application is complete and accurate and is not false or misleading;

(d) the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of any research ethics board that has previously refused to approve the protocol referred to in paragraph (a), its reasons for doing so and the date on which the refusal was given, if known at the time of submitting the application;

(e) an investigator's brochure that contains the following information, namely,

(i) the physical, chemical and pharmaceutical properties of the drug,

(ii) the pharmacological aspects of the drug, including its metabolites in all animal species tested,

(iii) the pharmacokinetics of the drug and the drug metabolism, including the biological transformation of the drug in all animal species tested,

(iv) any toxicological effects in any animal species tested under a single dose study, a repeated dose study or a special study in respect of the drug,

(v) any results of carcinogenicity studies in any animal species tested in respect of the drug,

(vi) any results of clinical pharmacokinetic studies of the drug,

(vii) any information regarding drug safety, pharmacodynamics, efficacy and dose responses of the drug that were obtained from previous clinical trials in humans, and

(viii) if the drug is a radiopharmaceutical as defined in section C.03.201, information regarding directions for preparing the radiopharmaceutical, the radiation dosimetry in respect of the prepared radiopharmaceutical and a statement of the storage requirements for the prepared radiopharmaceutical;

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(f) if the drug contains a human-sourced excipient, including any used in the placebo,

(i) information that indicates the human-sourced excipient has been assigned a drug identification number under subsection C.01.014.2(1) or, in the case of a new drug, issued a notice of compliance under subsection C.08.004(1), as the case may be, or

(ii) in any other case, sufficient information to support the identify, purity, potency, stability and safety of the human-sourced excipient;

(g) if the drug has not been assigned a drug identification number under subsection C.01.014.2(1) or, in the case of a new drug, a notice of compliance has not been issued under subsection C.08.004(1), the chemistry and manufacturing information in respect of the drug, including its site of manufacture; and

(h) the proposed date for the commencement of the clinical trial at each clinical trial site, if known at the time of submitting the application.

Authorization

C.05.006. (1) Subject to subsection (3), a sponsor may sell or import a drug, other than a drug described in subsection (2), for the purposes of a clinical trial if

(a) the sponsor has submitted to the Minister an application in accordance with section C.05.005;

(b) the Minister does not, within 30 days after the date of receipt of the application, send to the sponsor a notice in respect of the drug indicating that the sponsor may not sell or import the drug for any of the following reasons:

(i) that the information and documents in respect of the application

(A) were not provided in accordance with these Regulations, or

(B) are insufficient to enable the Minister to assess the safety and risks of the drug or the clinical trial, or

(ii) that based on an assessment of the application, an assessment of any information submitted under section C.05.009 or a review of any other information, the Minister has reasonable grounds to believe that

(A) the use of the drug for the purposes of the clinical trial endangers the health of a clinical trial subject or other person,

(B) the clinical trial is contrary to the best interests of a clinical trial subject, or

(C) the objectives of the clinical trial will not be achieved;

(c) for each clinical trial site, the sponsor has obtained the approval of the research ethics board in respect of the protocol referred to in paragraph C.05.005(a) and in respect of an informed consent form that contains the statement referred to in paragraph C.05.005(b); and

(d) before the sale or importation of the drug at a clinical trial site, the sponsor submits to the Minister the information referred to in subparagraphs C.05.005(c)(ix) and (x) and paragraphs C.05.005(d) and (h), if it was not submitted in respect of that clinical trial site at the time of submitting the application.

(2) Subject to subsection (3), a sponsor may sell or import a drug for the purposes of a clinical trial in respect of

(a) a new drug that has been issued a notice of compliance under subsection C.08.004(1), if the clinical tria is in respect of a purpose or condition of use for which the notice of compliance was issued; or

(b) a drug, other than a new drug, that has been assigned a drug identification number under subsection C.01.014.2(1), if the clinical trial is in respect of a use or purpose for which the drug identification number was assigned.

(3) A sponsor may not sell or import a drug for the purposes of a clinical trial

(a) during the period of any suspension made under section C.05.016 or C.05.017; or

(b) after a cancellation made under section C.05.016 or C.05.017.

Notification

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C.05.007. If the sale or importation of a drug is authorized under this Division, the sponsor may make one or more of the following changes if the sponsor notifies the Minister in writing within 15 days after the date of the change:

(a) a change to the chemistry and manufacturing information that does not affect the quality or safety of the drug, other than a change for which an amendment is required by section C.05.008; and

(b) a change to the protocol that does not alter the risk to the health of a clinical trial subject, other than a change for which an amendment is required by section C.05.008.

Amendment

C.05.008. (1) Subject to subsections (4) and (5), when the sale or importation of a drug is authorized under this Division and the sponsor proposes to make an amendment referred to in subsection (2), the sponsor may sell or import the drug for the purposes of the clinical trial in accordance with the amended authorization, if the following conditions are met:

(a) the sponsor has submitted to the Minister an application for amendment in accordance with subsection (3);

(b) the Minister does not, within 30 days after the date of receipt of the application for amendment, send to the sponsor a notice in respect of the drug indicating that the sponsor may not sell or import the drug in accordance with the amendment for any of the following reasons, namely,

(i) that the information and documents in respect of the application for amendment

(A) were not provided in accordance with these Regulations, or

(B) are insufficient to enable the Minister to assess the safety and risks of the drug or the clinical trial, or

(ii) that based on an assessment of the application for amendment, an assessment of any information submitted under section C.05.009 or a review of any other information, the Minister has reasonable grounds to believe that

(A) the use of the drug for the purposes of the clinical trial endangers the health of a clinical trial subject or other person,

(B) the clinical trial is contrary to the best interests of a clinical trial subject, or

(C) the objectives of the clinical trial will not be achieved;

(c) before the sale or importation of the drug, the sponsor submits to the Minister

(i) for each clinical trial site, the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of the research ethics board that approved any amended protocol submitted under paragraph (3)(a) or approved any amended statement submitted under paragraph (3)(c), and

(ii) the name, address and telephone number and, if applicable, the facsimile number and electronic mail address of any research ethics board that has previously refused to approve any amendment to the protocol, its reasons for doing so and the date on which the refusal was given;

(d) before the sale or importation of the drug, the sponsor maintains records concerning

(i) the information referred to in paragraph C.05.005(h), and

(ii) the information referred to in subparagraph C.05.005(c)(ix), if any of that information has changed since it was submitted;

(e) before the sale or importation of the drug in accordance with the amended authorization, the sponsor ceases to sell or import the drug in accordance with the existing authorization; and

(f) the sponsor conducts the clinical trial in accordance with the amended authorization.

(2) For the purposes of subsection (1), amendments are

(a) amendments to the protocol that affect the selection, monitoring or dismissal of a clinical trial subject;
(b) amendments to the protocol that affect the evaluation of the clinical efficacy of the drug;
(c) amendments to the protocol that alter the risk to the health of a clinical trial subject;
(d) amendments to the protocol that affect the safety evaluation of the drug;
(e) amendments to the protocol that extend the duration of the clinical trial; and
7-6-01 (f) amendments to the chemistry and manufacturing information that may affect the safety or quality of the drug.

(3) The application for amendment referred to in subsection (1) shall contain a reference to the application submitted under section C.05.005 and shall contain the following documents and information:

(a) if the application is in respect of an amendment referred to in any of paragraphs (2)(a) to (e), a copy of the amended protocol that indicates the amendment, a copy of the protocol submitted under paragraph C.05.005(a), and the rationale for the amendment;

(b) if the application is in respect of an amendment referred to in paragraph (2)(e), a copy of the amended investigator's brochure or an addendum to the investigator's brochure that indicates the new information, including supporting toxicological studies and clinical trial safety data;

(c) if the application is in respect of an amendment referred to in any of paragraphs (2)(a) to (f) and, as a result of that amendment, it is necessary to amend the statement referred to in paragraph C.05.005(b), a copy of the amended statement that indicates the new information; and

(d) if the application is in respect of an amendment referred to in paragraph (2)(f), a copy of the amended chemistry and manufacturing information that indicates the amendment, and the rationale for that amendment.

(4) If the sponsor is required to immediately make one or more of the amendments referred to in subsection (2) because the clinical trial or the use of the drug for the purposes of the clinical trial endangers the health of a clinical trial subject or other person, the sponsor may immediately make the amendment and shall provide the Minister with the information referred to in subsection (3) within 15 days after the date of the amendment.

(5) A sponsor may not sell or import a drug for the purposes of a clinical trial

(a) during the period of any suspension made under section C.05.016 or C.05.017; or

(b) after a cancellation made under section C.05.016 or C.05.017.

Additional Information and Samples

C.05.009. If the information and documents submitted in respect of an application under section C.05.005 o an application for amendment under section C.05.008 are insufficient to enable the Minister to determine whether any of the reasons referred to in paragraph C.05.006(1)(b) or C.05.008(1)(b) exist, the Minister may require the sponsor to submit, within two days after receipt of the request, samples of the drug or additional information relevant to the drug or the clinical trial that are necessary to make the determination.

Sponsor's Obligations

Good Clinical Practices

C.05.010. Every sponsor shall ensure that a clinical trial is conducted in accordance with good clinical practices and, without limiting the generality of the foregoing, shall ensure that

(a) the clinical trial is scientifically sound and clearly described in a protocol;

(b) the clinical trial is conducted, and the drug is used, in accordance with the protocol and this Division;

(c) systems and procedures that assure the quality of every aspect of the clinical trial are implemented;

(d) for each clinical trial site, the approval of a research ethics board is obtained before the clinical trial begins at the site;

(e) at each clinical trial site, there is no more than one qualified investigator;

(f) at each clinical trial site, medical care and medical decisions, in respect of the clinical trial, are under the supervision of the qualified investigator;

(g) each individual involved in the conduct of the clinical trial is qualified by education, training and experience to perform his or her respective tasks;

(h) written informed consent, given in accordance with the applicable laws governing consent, is obtained from every person before that person participates in the clinical trial but only after that person has been informed of

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(i) the risks and anticipated benefits to his or her health arising from participation in the clinical trial, and

(ii) all other aspects of the clinical trial that are necessary for that person to make the decision to participate in the clinical trial;

(i) the requirements respecting information and records set out in section C.05.012 are met; and

(j) the drug is manufactured, handled and stored in accordance with the applicable good manufacturing practices referred to in Divisions 2 to 4 except sections C.02.019, C.02.025 and C.02.026.

Labelling

C.05.011. Despite any other provision of these Regulations respecting labelling, the sponsor shall ensure tha the drug bears a label that sets out the following information in both official languages:

(a) a statement indicating that the drug is an investigational drug to be used only by a qualified investigator;

(b) the name, number or identifying mark of the drug;

(c) the expiration date of the drug;

(d) the recommended storage conditions for the drug;

(e) the lot number of the drug;

(f) the name and address of the sponsor;

(g) the protocol code or identification; and

(h) if the drug is a radiopharmaceutical as defined in section C.03.201, the information required by subparagraph C.03.202(1)(b)(vi).

Records

C.05.012. (1) The sponsor shall record, handle and store all information in respect of a clinical trial in a way that allows its complete and accurate reporting as well as its interpretation and verification.

(2) The sponsor shall maintain complete and accurate records to establish that the clinical trial is conducted in accordance with good clinical practices and these Regulations.

(3) The sponsor shall maintain complete and accurate records in respect of the use of a drug in a clinical trial, including

(a) a copy of all versions of the investigator's brochure for the drug;

(b) records respecting each change made to the investigator's brochure, including the rationale for each change and documentation that supports each change;

(c) records respecting all adverse events in respect of the drug that have occurred inside or outside Canada, including information that specifies the indication for use and the dosage form of the drug at the time of the adverse event;

(d) records respecting the enrolment of clinical trial subjects, including information sufficient to enable all clinical trial subjects to be identified and contacted in the event that the sale of the drug may endanger the health of the clinical trial subjects or other persons;

(e) records respecting the shipment, receipt, disposition, return and destruction of the drug;

(f) for each clinical trial site, an undertaking from the qualified investigator that is signed and dated by the qualified investigator prior to the commencement of his or her responsibilities in respect of the clinical trial, that states that

(i) the qualified investigator will conduct the clinical trial in accordance with good clinical practices, and

(ii) the qualified investigator will immediately, on discontinuance of the clinical trial by the sponsor, i its entirety or at a clinical trial site, inform both the clinical trial subjects and the research ethics board of the discontinuance, provide them with the reasons for the discontinuance and advise them in writing of any potential risks to the health of clinical trial subjects or other persons;

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(g) for each clinical trial site, a copy of the protocol, informed consent form and any amendment to the protocol or informed consent form that have been approved by the research ethics board for that clinical trial site; and

(h) for each clinical trial site, an attestation, signed and dated by the research ethics board for that clinical trial site, stating that it has reviewed and approved the protocol and informed consent form and that the board carries out its functions in a manner consistent with good clinical practices.

(4) The sponsor shall maintain all records referred to in this Division for a period of 25 years.

Submission of Information and Samples

C.05.013. (1) The Minister shall require a sponsor to submit, within two days after receipt of the request, information concerning the drug or the clinical trial, or samples of the drug, if the Minister has reasonable grounds to believe that

(a) the use of the drug for the purposes of the clinical trial endangers the health of a clinical trial subject or other person;

(b) the clinical trial is contrary to the best interests of a clinical trial subject;

(c) the objectives of the clinical trial will not be achieved;

(d) a qualified investigator is not respecting the undertaking referred to in paragraph C.05.012(3)(f); or

(e) information submitted in respect of the drug or the clinical trial is false or misleading.

(2) The Minister may require the sponsor to submit, within seven days after receipt of the request, any information or records kept under section C.05.012, or samples of the drug, in order to assess the safety of the drug or the health of clinical trial subjects or other persons.

Serious Unexpected Adverse Drug Reaction Reporting

C.05.014. (1) During the course of a clinical trial, the sponsor shall inform the Minister of any serious unexpected adverse drug reaction in respect of the drug that has occurred inside or outside Canada as follows:

(a) if it is neither fatal nor life threatening, within 15 days after becoming aware of the information; and

(b) if it is fatal or life threatening, within seven days after becoming aware of the information.

(2) The sponsor shall, within eight days after having informed the Minister under paragraph (1)(b), submit to the Minister a complete report in respect of that information that includes an assessment of the importance and implication of any findings made.

(3) Sections C.01.016 and C.01.017 do not apply to drugs used for the purposes of a clinical trial.

Discontinuance of a Clinical Trial

C.05.015. (1) If a clinical trial is discontinued by the sponsor in its entirety or at a clinical trial site, the sponsor shall

(a) inform the Minister no later than 15 days after the date of the discontinuance;

(b) provide the Minister with the reason for the discontinuance and its impact on the proposed or ongoing clinical trials in respect of the drug conducted in Canada by the sponsor;

(c) as soon as possible, inform all qualified investigators of the discontinuance and of the reasons for the discontinuance, and advise them in writing of any potential risks to the health of clinical trial subjects or other persons; and

(d) in respect of each discontinued clinical trial site, stop the sale or importation of the drug as of the date o the discontinuance and take all reasonable measures to ensure the recovery of all unused quantities of the drug that have been sold.

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(2) If the sponsor has discontinued the clinical trial in its entirety or at a clinical trial site, the sponsor may resume selling or importing the drug for the purposes of a clinical trial in its entirety or at a clinical trial site if, in respect of each clinical trial site where the sale or importation is to be resumed, the sponsor submits to the Minister the information referred to in subparagraphs C.05.005(c)(ix) and (x) and paragraphs C.05.005(d) and (h).

Suspension and Cancellation

C.05.016. (1) Subject to subsection (2), the Minister shall suspend the authorization to sell or import a dru for the purposes of a clinical trial, in its entirety or at a clinical trial site, if the Minister has reasonable grounds to believe that

(a) the sponsor has contravened these Regulations of any provisions of the Act relating to the drug;

(b) any information submitted in respect of the drug or clinical trial is false or misleading;

(c) the sponsor has failed to comply with good clinical practices; or

(d) the sponsor has failed to provide
(i) information or samples of the drug as required under section C.05.009 or C.05.013, or
(ii) information or a report under section C.05.014.

(2) Subject to section C.05.017, the Minister shall not suspend an authorization referred to in subsection (1) unless

(a) the Minister has sent to the sponsor a written notice of the intention to suspend the authorization that indicates whether the authorization is to be suspended in its entirety or at a clinical trial site and the reason for the intended suspension;

(b) the sponsor has not, within 30 days after receipt of the notice referred to in paragraph (a), provided the Minister with information or documents that demonstrate that the authorization should not be suspended on the grounds that
(i) the situation giving rise to the intended suspension did not exist, or
(ii) the situation giving rise to the intended suspension has been corrected; and

(c) the Minister has provided the sponsor with the opportunity to be heard in paragraph (b).

(3) The Minister shall suspend the authorization by sending to the sponsor a written notice of suspension of the authorization that indicates the effective date of the suspension, whether the authorization is suspended in its entirety or at a clinical trial site and the reason for the suspension.

(4) If the Minister has suspended an authorization, the Minister shall

(a) reinstate the authorization in its entirety or at a clinical trial site, as the case may be, if within 30 days after the effective date of the suspension the sponsor provides the Minister with information or documents that demonstrate that the situation giving rise to the suspension has been corrected; or

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(b) cancel the authorization in its entirety or at a clinical trial site, as the case may be, if within 30 days after the effective date of the suspension the sponsor has not provided the Minister with the information or documents referred to in paragraph (a).

C.05.017. (1) The Minister shall suspend an authorization to sell or import a drug for the purposes of a clinical trial, in its entirety or at a clinical trial site, before giving the sponsor an opportunity to be heard if the Minister has reasonable grounds to believe that it is necessary to do so to prevent injury to the health of a clinical trial subject or other person.

(2) The Minister shall suspend the authorization by sending to the sponsor a written notice of suspension of the authorization that indicates the effective date of the suspension, whether the authorization is suspended in its entirety or at a clinical trial site and the reason for the suspension.

(3) If the Minister has suspended an authorization, the Minister shall

(a) reinstate the authorization in its entirety or at a clinical trial site, as the case may be, if within 60 days after the effective date of the suspension the sponsor provides the Minister with information or documents that demonstrate that the situation giving rise to the suspension did not exist or that it has been corrected; or

(b) cancel the authorization in its entirety or at a clinical trial site, as the case may be, if within 60 days after the effective date of the suspension the sponsor has not provided the Minister with the information or documents referred to in paragraph (a).

Canadian Standard Drugs

Conjugated Estrogens
Conjugated Estrogens for Injection
Conjugated Estrogens Tablets
Digitoxin
Digitoxin Tablets
Digoxin
Digoxin Elixir
Digoxin Injection
Digoxin Tablets
Esterified Estrogens
Esterified Estrogens Tablets
Gelatin
Thyroid

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General

C.06.001. In this Division

(a) solubility and specific gravity shall be determined at 25°C,
1-12-77 (b) Revoked by P.C. 1977-3383 of December 1, 1977
(c) tests for identity, quantitative tests for arsenic, lead, copper, zinc, fluorine, and sulphur dioxide, and limit tests shall be made by acceptable methods, and
(d) determination of physical and chemical constants shall be carried out by acceptable methods.

Conjugated Estrogens

C.06.002. [S]. Conjugated estrogens shall be the drug conjugated estrogens described in The Pharmacopeia of the United States of America, XVIII (1970), except that

(a) the dilute assay preparation A, assay preparations A and B and equilin reagent described therein shall be prepared by official method DO-29, Conjugated Estrogens, October 15, 1981; and
23-4-82 (b) the identification test described therein shall be performed by official method DO-29, Conjugated Estrogens, October 15, 1981.

Conjugated Estrogens for Injection

10-11-76 **C.06.003. [S]. Conjugated estrogens for injection** shall be the drug conjugated estrogens for injection described in The Pharmacopeia of the United States of America, XVIII (1970), except that

(a) the dilute assay preparation A, assay preparations A and B and equilin reagent described therein shall be prepared by official method DO-29, Conjugated Estrogens, October 15, 1981; and
23-4-82 (b) the identification test described therein shall be performed by official method DO-29, Conjugated Estrogens, October 15, 1981.

Conjugated Estrogens Tablets

C.06.004. [S]. Conjugated estrogens tablets shall be the drug conjugated estrogens tablets described in The Pharmacopeia of the United States of America, XVIII (1970), except that

(a) the dilute assay preparation A, assay preparations A and B and equilin reagent described therein shall be prepared by official method DO-29, Conjugated Estrogens, October 15, 1981; and
23-4-82 (b) the identification test described therein shall be performed by official method DO-29, Conjugated Estrogens, October 15, 1981.

C.06.100. Revoked by P.C. 1980-1850 of July 10, 1980.

C.06.101. Revoked by P.C. 1980-1850 of July 10, 1980.

Digitoxin

23-6-71 **C.06.120. [S]. Digitoxin** shall be the drug digitoxin described in the Pharmacopeia of the United States of America.

Sections C.06.121 and C.06.122 are revoked by P.C. 1971-1258 of June 23, 1971.

Digitoxin Tablets

24-5-72 **C.06.121. [S].** Digitoxin tablets shall be the drug digitoxin tablets described in the Pharmacopeia of the United States of America.

Digoxin

C.06.130. [S]. Digoxin shall be the drug digoxin described in the Pharmacopeia of the United States of America.

Digoxin Elixir

C.06.131. [S]. Digoxin Elixir shall be the drug digoxin elixir described in the Pharmacopeia of the United State of America.

Digoxin Injection

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C.06.132. [S]. Digoxin injection shall be the drug digoxin injection described in the Pharmacopeia of the United States of America.

Digoxin Tablets

C.06.133. [S]. Digoxin tablets shall be the drug digoxin tablets described in the Pharmacopeia of the United States of America.

Sections C.06.140, C.06.141, C.06.142, C.06.150, C.06.151, C.06.153, C.06.154, C.06.155, C.06.156 are revoked by P.C. 1980-1850 of July 10, 1980.

C.06.157. Revoked by P.C. 1980-1850 of July 10, 1980.

C.06.158. Revoked by P.C. 1980-1850 of July 10, 1980.

C.06.159. Revoked by P.C. 1980-1850 of July 10, 1980.

C.06.160. Revoked by P.C. 1980-1850 of July 10, 1980.

Esterified Estrogens

9-11-71 | **C.06.161. [S]. Esterified estrogens** shall be the drug esterified estrogens described in the Pharmacopeia of the United States of America.

Esterified Estrogens Tablets

23-6-71 | **C.06.162. [S]. Esterified estrogens tablets** shall be the drug esterified estrogens tablets described in the Pharmacopeia of the United States of America.

Gelatin

1-12-77 **C.06.170.** Gelatin shall be the drug gelatin described in the Pharmacopeia of the United States or the British Pharmacopeia.

C.06.180. Revoked by P.C. 1980-1850 of July 10, 1980.

C.06.181. Revoked by P.C. 1980-1850 of July 10, 1980.

Sections C.06.182, C.06.183, C.06.230, C.06.231, C.06.232, C.06.233, C.06.240, C.06.241, C.06.242 are revoked by P.C. 1980-1850 of July 10, 1980.

Thyroid

C.06.250. **Thyroid** shall be the cleaned, dried, powdered thyroid glands of domestic animals used for food, and shall contain not less than 0.17 per cent, and not more than 0.23 per cent iodine and no added iodine in either inorganic or organic form, and

(a) its characters are

Description,--

(i) General--thyroid occurs as a cream-coloured, amorphous powder; the odour and taste are faint and meat-like, and

(ii) Microscopical,--when suitably mounted and examined under the microscope, thyroid shows the following: numerous smooth to striated hyaline fragments of colloids, of angular to irregular shape, that are colourless to pale yellow in water mounts, brown in Mallory's stain and pink in solution of casin, some of these fragments containing granules, minute vacuoles, crystalloidal bodies and cells; numerous irregular fragments of folicular epithelium staining brown with Mallory's stain, the individual cells more or less polygonal to rounded-angular or irregularly cuboidal, often with prominent nuclei staining dark blue, their cytoplasm purplish with Delafield's solution of haematoxylin; slender glistening segments of capillaries of closely undulate outline; numerous slender segments of neuraxons; numerous aggregates of particles of intercellular substance and slender, mostly straight connective tissue fibres staining blue to greenish blue with a mixture of Mallory's stain and solution of phosphotungstic acid, the bundles of fibres often appearing reddish in Mallory's stain few glistening fragments of blood vessels with serrated or crenated ends as viewed in water mounts, and

(b) the test for its purity are

(i) Inorganic iodine--add to 1 gram of thyroid 10 millilitres of a saturated solution of zinc sulphate in water, shake, allow to stand 5 minutes, and filter through a fritted glass filter; add to 5 millilitres of the filtrate 0.5 millilitre of mucilage of starch and 4 drops each of a 10 per cent w/v solution of sodium nitrite in water and dilute sulphuric acid, shaking after each addition: no blue colour is produced, and

(ii) Moisture,--thyroid loses not more than 6 per cent moisture.

C.06.251. Thyroid shall be

23-4-82

(a) assayed by official method DO-26, Thyroid, October 15, 1981; and

(b) stored in a cool place and in a tightly-closed container.

Sections C.06.252, C.06.260, C.06.261, C.06.262, C.06.263, C.06.264, C.06.270, C.06.271, C.06.272, C.06.273, C.06.274, C.06.275, C.06.276, C.06.277, C.06.278, C.06.279, C.06.280 are revoked by P.C. 1980-1850 of July 10, 1980.

ANNEX TO DIVISION 6

Revoked by P.C. 1977-3383 of December 1, 1977

DIVISION 7

Revoked by P.C. 1984-2591 of July 18, 1984

(Section C.07.004, C.07.005 and C.07.006 and heading preceding section C.07.004 are revoked).

500

New Drugs

4-4-95 **C.08.001.** For the purposes of the Act and this Division, "new drug" means

(a) a drug that contains or consists of a substance, whether as an active or inactive ingredient, carrier, coating, excipient, menstruum or other component, that has not been sold as a drug in Canada for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that substance for use a a drug;

(b) a drug that is a combination of two or more drugs, with or without other ingredients, and that has not been sold in that combination or in the proportion in which those drugs are combined in that drug, for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that combination and proportion for use as a drug; or

(c) a drug, with respect to which the manufacturer prescribes, recommends, proposes or claims a use as a drug, or a condition of use as a drug, including dosage, route of administration, or duration of action and that has not been sold for that use or condition of use in Canada, for sufficient time and in sufficient quantity to establish in Canada the safety and effectiveness of that use or condition of use of that drug.

C.08.001.1. For the purposes of this Division,

"Canadian reference product" means

(a) a drug in respect of which a notice of compliance is issued pursuant to section C.08.004 and which is marketed in Canada by the innovator of the drug,

(b) a drug, acceptable to the Minister, that can be used for the purpose of demonstrating bioequivalence on the basis of pharmaceutical and, where applicable, bioavailability characteristics, where a drug in respect of which a notice of compliance has been issued pursuant to section C.08.004 cannot be used for that purpose because it is no longer marketed in Canada, or

16-8-95 (c) a drug, acceptable to the Minister, that can be used for the purpose of demonstrating bioequivalence on the basis of pharmaceutical and, where applicable, bioavailability characteristics, in comparison to a drug referred to in paragraph (a); (produit de référence canadien)

"pharmaceutical equivalent" means a new drug that, in comparison with another drug, contains identical amounts of the identical medicinal ingredients, in comparable dosage forms, but that does not necessarily contain the same non-medicinal ingredients; (équivalent pharmaceutique)

"specifications" means a detailed description of a new drug and of its ingredients and includes

(a) a statement of all properties and qualities of the ingredients that are relevant to the manufacture and use of the new drug, including the identity, potency and purity of the ingredients,

(b) a detailed description of the methods used for testing and examining the ingredients, and

(c) a statement of the tolerances associated with the properties and qualities of the ingredients. (spécifications)

C.08.002. (1) No person shall sell or advertise a new drug unless

(a) the manufacturer of the new drug has filed with the Minister a new drug submission or an abbreviated new drug submission relating to the new drug that is satisfactory to the Minister;

16-8-95 (b) the Minister has issued, pursuant to section C.08.004, a notice of compliance to the manufacturer of the new drug in respect of the new drug submission or abbreviated new drug submission;

(c) the notice of compliance in respect of the submission has not been suspended pursuant to section C.08.006; and

(d) the manufacturer of the new drug has submitted to the Minister specimens of the final version of any labels, including package inserts, product brochures and file cards, intended for use in connection with that new drug, and a statement setting out the proposed date on which those labels will first be used.

16-8-95 (2) A new drug submission shall contain sufficient information and material to enable the Minister to assess the safety and effectiveness of the new drug, including the following:

20-4-93 (a) a description of the new drug and a statement of its proper name or its common name if there is no proper name;

(b) a statement of the brand name of the new drug or the identifying name or code proposed for the new drug;

(c) a list of the ingredients of the new drug, stated quantitatively, and the specifications for each of those ingredients;

16-8-95 (d) a description of the plant and equipment to be used in the manufacture, preparation and packaging of the new drug;

(e) details of the method of manufacture and the controls to be used in the manufacture, preparation and packaging of the new drug;

(f) details of the tests to be applied to control the potency, purity, stability and safety of the new drug;
(g) detailed reports of the tests made to establish the safety of the new drug for the purpose and under the conditions of use recommended;
(h) substantial evidence of the clinical effectiveness of the new drug for the purpose and under the conditions of use recommended;
20-4-93 (i) a statement of the names and qualifications of all the investigators to whom the new drug has been sold;
(j) a draft of every label to be used in conjunction with the new drug;
(k) a statement of all the representations to be made for the promotion of the new drug respecting
(i) the recommended route of administration of the new drug,
(ii) the proposed dosage of the new drug,
(iii) the claims to be made for the new drug, and
(iv) the contra-indications and side effects of the new drug;
(l) a description of the dosage form in which it is proposed that the new drug be sold;
16-8-95 (m) evidence that all test batches of the new drug used in any studies conducted in connection with the submission were manufactured and controlled in a manner that is representative of market production; and
(n) for a drug intended for administration to food-producing animals, the withdrawal period of the new drug.

(3) The manufacturer of a new drug shall, at the request of the Minister, provide the Minister, where for the purposes of a new drug submission the Minister considers it necessary to assess the safety and effectiveness of the new drug, with the following information and material:

16-8-95 (a) the names and addresses of the manufacturers of each of the ingredients of the new drug and the name and addresses of the manufacturers of the new drug in the dosage form in which it is proposed that the new drug be sold;
(b) samples of the ingredients of the new drug;
(c) samples of the new drug in the dosage form in which it is proposed that the new drug be sold; and
(d) any additional information or material respecting the safety and effectiveness of the new drug.

C.08.002.1. (1) A manufacturer of a new drug may file an abbreviated new drug submission for the new drug where, in comparison with a Canadian reference product,

(a) the new drug is the pharmaceutical equivalent of the Canadian reference product;
(b) the new drug is bioequivalent with the Canadian reference product, based on the pharmaceutical and, where the Minister considers it necessary, bioavailability characteristics;
(c) the route of administration of the new drug is the same as that of the Canadian reference product; and
(d) the conditions of use for the new drug fall within the conditions of use for the Canadian reference product.

(2) An abbreviated new drug submission shall contain sufficient information and material to enable the Minister to assess the safety and effectiveness of the new drug, including the following:

(a) the information and material described in paragraphs C.08.002(2)(a) to (f) and (j) to (l);
(b) information identifying the Canadian reference product used in any comparative studies conducted in connection with the submission;
16-8-95 (c) evidence from the comparative studies conducted in connection with the submission that the new drug is
(i) the pharmaceutical equivalent of the Canadian reference product, and
(ii) where the minister considers it necessary on the basis of the pharmaceutical and, where applicable, bioavailability characteristics of the new drug, bioequivalent with the Canadian reference product as demonstrated using bioavailability studies, pharmacodynamic studies or clinical studies;
(d) evidence that all test batches of the new drug used in any studies conducted in connection with the submission were manufactured and controlled in a manner that is representative of market production; and
(e) for a drug intended for administration to food-producing animals, sufficient information to confirm that the withdrawal period is identical to that of the Canadian reference product.

(3) The manufacturer of a new drug shall, at the request of the Minister, provide the Minister, where for the purposes of an abbreviated new drug submission the Minister considers it necessary to assess the safety and effectiveness of the new drug, with the following information and material:

(a) the names and addresses of the manufacturers of each of the ingredients of the new drug and the name and addresses of the manufacturers of the new drug in the dosage form in which it is proposed that the new drug be sold;
(b) samples of the ingredients of the new drug;
(c) samples of the new drug in the dosage form in which it is proposed that the new drug be sold; and
(d) any additional information or material respecting the safety and effectiveness of the new drug.

C.08.003. (1) Notwithstanding section C.08.002, no person shall sell a new drug in respect of which a notic of compliance has been issued to the manufacturer of that new drug and has not been suspended pursuant to section C.08.006, if any of the matters specified in subsection (2) are significantly different from the information or material contained in the new drug submission or abbreviated new drug submission, unless

(a) the manufacturer of the new drug has filed with the Minister
  (i) a supplement to that new drug submission, or
  (ii) a supplement to that abbreviated new drug submission;
(b) the Minister has issued a notice of compliance to the manufacturer of the new drug in respect of the supplement;
(c) the notice of compliance in respect of the supplement has not been suspended pursuant to section C.08.006; and
(d) the manufacturer of the new drug has submitted to the Minister specimens of the final version of any label, including any package insert, product brochure and file card, intended for use in connection with the new drug, where a change with respect to any of the matters specified in subsection (2) is made that would require a change to the label.

(2) The matters specified for the purposes of subsection (1), in relation to the new drug, are the following:

(a) the description of the new drug;
(b) the brand name of the new drug or the identifying name or code proposed for the new drug;
16-8-95 (c) the specifications of the ingredients of the new drug;
(d) the plant and equipment used in manufacturing, preparation and packaging the new drug;
(e) the method of manufacture and the controls used in manufacturing, preparation and packaging the new drug;
(f) the tests applied to control the potency, purity, stability and safety of the new drug;
(g) the labels used in connection with the new drug;
(h) the representations made with regard to the new drug respecting
  (i) the recommended route of administration of the new drug,
  (ii) the dosage of the new drug,
  (iii) the claims made for the new drug,
  (iv) the contra-indications and side effects of the new drug, and
  (v) the withdrawal period of the new drug; and
(i) the dosage form in which it is proposed that the new drug be sold.

(3) A supplement to a new drug submission or to an abbreviated new drug submission, with respect to the matters that are significantly different from those contained in the submission, shall contain sufficient information and material to enable the Minister to assess the safety and effectiveness of the new drug in relation to those matters.

7-6-01 **C.08.003.1.** The Minister may examine any information or material filed with the Minister by any person pursuant to Division 5 or section C.08.002, C.08.002.1, C.08.003, C.08.005 or C.08.005.1 to establish the safety and effectiveness of the new drug for which the submission or supplement has been filed.

C.08.004. (1) Subject to section C.08.004.1, the Minister shall, after completing an examination of a new drug submission or abbreviated new drug submission or a supplement to either submission,

(a) if that submission or supplement complies with section C.08.002, C.08.002.1 or C.08.003, as the case may be, and section C.08.005.1, issue a notice of compliance; or
16-8-95 (b) if that submission or supplement does not comply with section C.08.002, C.08.002.1 or C.08.003, as the case may be, or section C.08.005.1, notify the manufacturer that the submission or supplement does no so comply.

(2) Where a new drug submission or abbreviated new drug submission or a supplement to either submission does not comply with section C.08.002, C.08.002.1 or C.08.003, as the case may be, or section C.08.005.1, the manufacturer who filed the submission or supplement may amend the submission or supplement by filing additional information or material.

(3) Subject to section C.08.004.1, the Minister shall, after completing an examination of any additional information or material filed in respect of a new drug submission or an abbreviated new drug submission or a supplement to either submission,

(a) if that submission or supplement complies with section C.08.002, C.08.002.1 or C.08.003, as the case may be, and section C.08.005.1, issue a notice of compliance; or
(b) if that submission or supplement does not comply with the requirements of section C.08.002, C.08.002. or C.08.003, as the case may be, or section C.08.005.1, notify the manufacturer that the submission or supplement does not so comply.

(4) A notice of compliance issued in respect of a new drug on the basis of information and material contained in a submission filed pursuant to section C.08.002.1 shall state the name of the Canadian reference product referred to in the submission and shall constitute a declaration of equivalence for that new drug.

16-8-95 **C.08.004.1.** (1) Where a manufacturer files a new drug submission, an abbreviated new drug submission, a supplement to a new drug submission or a supplement to an abbreviated new drug submission for the purpose of establishing the safety and effectiveness of the new drug for which the submission or supplement is filed, and the Minister examines any information of material filed with the Minister, in a new drug submission, by the innovator of a drug that contains a chemical or biological substance not previously approved for sale in Canada as a drug, and the Minister, in support of the manufacturer's submission or supplement, relies on data contained in the information or material filed by the innovator, the Minister shall not issue a notice of compliance in respect of that submission or supplement earlier than five years after the date of issuance to the innovator of the notice of compliance or approval to market that drug, as the case may be, issued on the basis of the information or material filed by the innovator for that drug.

(2) Subsection (1) does not apply where the manufacturer of a new drug for which a notice of compliance was issued pursuant to section C.08.004 gives written permission to another manufacturer to rely on the test or other data filed in respect of that new drug.

(3) Subsection (1) does not apply where the data relied upon by the Minister was contained in information or material filed by the innovator before January 1, 1994.

7-6-01 **C.08.005.** (1) Subject to subsection (1.1) and notwithstanding sections C.08.002 and C.08.003, a manufacturer of a new drug may sell it to a qualified investigator to be used solely for the purpose of clinical testing to obtain evidence with respect to the safety, dosage and effectiveness of that new drug, when the following conditions are met:

16-8-95 (a) before the sale, the manufacturer has filed with the Minister, in compliance with section C.08.005.1, a preclinical submission containing information and material respecting
20-4-93 (i) the brand name of the new drug or the identifying name or code proposed for the new drug,
(ii) the chemical structure or other specific identification of the composition of the new drug,
(iii) the source of the new drug,
(iv) a detailed protocol of the clinical testing,
(v) the results of investigations made to support the clinical use of the new drug,
(vi) the contra-indications and precautions known in respect of the new drug and the suggested treatment of overdosage of the new drug,
(vii) all ingredients of the new drug, stated quantitatively,
(viii) the methods, equipment, plant and controls used in the manufacture, processing and packaging o the new drug,
(ix) the tests applied to control the potency, purity and safety of the new drug, and
(x) the names and qualifications of all investigators to whom the drug is to be sold and the names of all institutions in which the clinical testing is to be carried out;
14-8-87 (b) the Director has not, within 60 days after the date of receipt of the preclinical submission, sent by registered mail to the manufacturer a notice in respect of that new drug indicating that the preclinical submission is not satisfactory;
(c) all inner labels and outer labels used in conjunction with the sale of the new drug to qualified investigators carry the statements
(i) "Investigational Drug" or "Drogue de recherche", and
(ii) "To Be Used By Qualified Investigators Only" or "Réservée uniquement à l'usage de chercheurs compétents";
(d) before the sale, the manufacturer ascertains that every qualified investigator to whom the new drug is to be sold
(i) has the facilities for the clinical testing to be conducted by the investigator, and
(ii) has received the information and material referred to in subparagraphs (a)(i) to (vi); and

(e) every qualified investigator to whom the new drug is to be sold has agreed in writing with the manufacturer that the investigator will
  (i) not use the new drug or permit it to be used other than for clinical testing,
  (ii) not permit the new drug to be used by any person other than the investigator except under the investigator's direction,
  (iii) report immediately to that manufacturer and, if so required by the Director, report to the Director all serious adverse reactions encountered during the clinical testing, and
  (iv) account to the manufacturer for all quantities of the new drug received, where so requested by the manufacturer.

7-6-01 (1.1) This section applied only in respect of a new drug for veterinary use.

(2) Notwithstanding subsection (1), no manufacturer shall sell a new drug to a qualified investigator unless that manufacturer has, in respect of all previous sales of that new drug to any qualified investigator,

(a) kept accurate records of the distribution of that new drug and of the results of the clinical testing and has made those records available to the Director for inspection on the request of the Director; and
(b) immediately reported to the Director all information he has obtained with respect to serious adverse reactions.

(3) The Minister may notify the manufacturer of a new drug that sales of that new drug to qualified investigators are prohibited if, in the opinion of the Minister, it is in the interest of public health to do so.

(4) Notwithstanding subsection (1), no manufacturer shall sell a new drug to a qualified investigator if the Minister has notified the manufacturer of that drug that such sales are prohibited.

14-8-87 (5) Paragraph (1)(c) does not apply to a radiopharmaceutical as defined in section C.03.201, or to a component or kit as defined in section C.03.205.

7-6-01 **C.08.005.1** (1) Every manufacturer who files a new drug submission, an abbreviated new drug submission, a supplement to a new drug submission, a supplement to an abbreviated new drug submission or a submissio for the clinical testing of a new drug for veterinary use shall, in addition to any information and material that is required under section C.08.002, C.08.003 and C.08.005, include in the submission or supplement

(a) a copy of all clinical case reports respecting any subject of a study included in the submission or supplement if that subject has died, suffered a serious adverse reaction or an unexpected adverse reaction, or the study, insofar as it relates to this subject, has not been completed;
(b) a sectional report in respect of each human, animal and in vitro study included in the submission or supplement;
(c) a comprehensive summary of each human, animal and in vitro study referred to or included in the submission or supplement; and
(d) a submission certificate in respect of all information and material contained in the submission or supplement and any additional information or material filed to amend the submission or supplement.

(2) A sectional report referred to in paragraph (1)(b) shall include
(a) a summary of each study included in the submission or supplement;
(b) a summary of any additional information or material filed to amend the submission or supplement; and
(c) where raw data is available to the manufacturer in respect of a study,
  (i) a summary of the data,
  (ii) a cross-referencing of the data to the relevant portions of the sectional report,
  (iii) a description of the conditions under which the experiments from which the data were obtained were conducted,
17-9-92 (iv) the details of the data treatment process, and
  (v) the results and conclusions of the study.

(3) The comprehensive summary referred to in paragraph (1)(c) shall include a summary of the methods used, results obtained and conclusions arrived at in respect of all studies referred to or included in the submission or supplement and shall be cross-referenced to the relevant portions of the section reports.

(4) The submission certificate referred to in paragraph (1)(d) shall
(a) certify that all information and material included in the submission or supplement and any additional information or material filed to amend the submission or supplement are accurate and complete, and that the sectional reports and the comprehensive summary correctly represent the information and material referred to or included in the submission or supplement; and
(b) be signed and dated by
  (i) the senior executive officer in Canada of the manufacturer filing the submission or supplement, and
  (ii) the senior medical or scientific officer of the manufacturer.

(5) No person shall sign a submission certificate if a sectional report, comprehensive summary or any information or material included in the submission or supplement, or any additional information and material filed to amend the submission or supplement,

(a) is false or misleading; or

(b) contains omissions that may affect its accuracy and completeness.

7-6-01 (6) Every manufacturer who has filed a new drug submission, an abbreviated new drug submission, a supplement to a new drug submission, a supplement to an abbreviated new drug submission or a submission for the clinical testing of a new drug for veterinary use, and has any relating clinical case reports or raw data that were not included therein, shall keep those reports or data and shall, within 30 days after receiving a written request from the Minister, submit them to the Minister.

7-6-01 **C.08.006.** (1) For the purposes of this section, evidence or new information obtained by the Minister includes any information or material filed by any person pursuant to Division 5 or section C.08.002, C.08.002.1, C.08.003, C.08.005 or C.08.005.1.

16-8-95 (2) The Minister may, by notice to a manufacturer, suspend, for a definite or indefinite period, a notice of compliance issued to that manufacturer in respect of a new drug submission or an abbreviated new drug submission or a supplement to either submission, if the Minister considers

(a) that the drug is not safe for the use represented in the submission or supplement, as shown by evidence obtained from

(i) clinical or other experience not reported in the submission or supplement or not available to the Minister at the time the notice of compliance was issued, or

(ii) tests by new methods or tests by methods not reasonably applicable at the time the notice of compliance was issued;

(b) that upon the basis of new information obtained after the issuance of the notice of compliance, there is lack of substantial evidence that the drug will have the effect it is represented to have under the conditions of use prescribed, recommended or proposed by the manufacturer;

16-8-95 (c) that the submission or supplement contained an untrue statement of material fact;

(d) that the manufacturer has failed to establish a system for maintaining required records or has repeatedly or deliberately failed to maintain such records;

10-10-63 (e) that, on the basis of new information obtained after the issuance of the notice of compliance, the methods, equipment, plant and controls used in the manufacturing, processing and packaging of the drug are inadequate to assure and preserve the identity, strength, quality or purity of the new drug; or

(f) that, on the basis of new information obtained after the issuance of the notice of compliance, the labelling of the drug is false or misleading or incomplete in any particular and that this defect was not corrected by the manufacturer upon receipt of a written notice from the Director specifying the respect in which the labelling is false or misleading or incomplete.

16-8-95 **C.08.007.** Where a manufacturer has received a notice of compliance issued in respect of a new drug submission or abbreviated new drug submission or a supplement to either submission, the manufacturer shall establish and maintain records, in a manner that enables an audit to be made, respecting

(a) animal or clinical experience, studies, investigations and tests conducted by the manufacturer or reported to him by any person concerning that new drug;

(b) reports from the scientific literature or the bibliography therefrom that are available to him concerning that new drug;

10-10-63 (c) experience, investigations, studies and tests involving the chemical or physical properties or any other properties of that new drug;

(d) any substitution of another substance for that new drug or any mixing of another substance with that new drug;

(e) any error in the labelling of that new drug or in the use of the labels designed for that new drug;

(f) any bacteriological or any significant chemical or physical or other change or deterioration in any lot of that new drug;

16-8-95 (g) any failure of one or more distributed lots of the new drug to meet the specifications established for that new drug in the submission or supplement; and

7-11-95 (h) any unusual failure in efficacy of that new drug.

C.08.008. No manufacturer shall sell a new drug unless the manufacturer has, with respect to all the manufacturer's previous sales of that new drug, furnished to the Minister

16-8-95 (a) on request, reports of all records respecting the information described in paragraphs C.08.007(a) to (c);

(b) immediately on receipt by the manufacturer, reports of all records respecting the information described in paragraphs C.08.007(d) to (f); and

7-11-95 (c) within 15 days after the receipt by the manufacturer of information referred to in paragraphs C.08.007(g) and (h), a report on the information received.

C.08.009. (1) Where the Minister has decided

7-6-01 (a) to notify the manufacturer of a new drug for veterinary use that the sale of that drug to qualified investigators is prohibitied, or

16-8-95 (b) to suspend a notice of compliance issued in respect of a new drug submission or an abbreviated new drug submission or a supplement to either submission,

the manufacturer, if dissatisfied with that decision, may require the Minister to provide him with the reasons for the decision.

(2) Where the manufacturer has received the reasons for a decision of the Minister pursuant to subsection (1), he may require the Minister to refer that decision to a New Drug Committee and thereupon shall provide the Minister with a statement of the reasons for his dissatisfaction and any information and material upon which he relies in support of those reasons.

(3) Where the Minister has been required to refer a decision to a New Drug Committee pursuant to subsection (2), he shall appoint a member of the New Drug Committee, the dissatisfied manufacturer shall appoint a member of the New Drug Committee and the two members so appointed shall appoint a third member of the New Drug Committee who shall be chairman, or, if they are unable to do so within a reasonable time, the Minister shall appoint a third member of the New Drug Committee who shall be chairman.

10-10-63 (4) Any person who is in the full-time employment of the Department or in the full-time employment of the dissatisfied manufacturer shall not be appointed a member of a New Drug Committee.

16-8-95 (4.1) A member of a New Drug Committee shall, on appointment, sign an undertaking not to disclose or use any information, material, data, evidence or representations considered pursuant to subsection (6).

(5) The Minister shall pay the reasonable fees and costs incurred by the member of the New Drug Committee appointed by the Minister, and the dissatisfied manufacturer shall pay the reasonable fees and costs incurred by the member appointed by the dissatisfied manufacturer, and the Minister and the dissatisfied manufacturer shall each pay half of the reasonable fees and costs incurred by the chairman.

10-10-63 (6) The New Drug Committee formed pursuant to subsection (3) shall consider the reasons for the decision of the Minister, the reasons for the dissatisfaction of the dissatisfied manufacturer and any information or material in support of the reasons of the Minister or the dissatisfied manufacturer and may consider other evidence, material, information or representations.

(7) The New Drug Committee formed pursuant to subsection (3) shall report its findings and recommendations to the Minister.

16-8-95 (7.1) No member of a New Drug Committee shall disclose or use any information, material, data, evidence or representations considered pursuant to subsection (6).

(8) Where the Minister has received the findings and recommendations of a New Drug Committee he may reconsider the decision to which those findings and recommendations relate.

Sale of New Drug for Emergency Treatment

C.08.010. (1) The Director may issue a letter of authorization authorizing the sale of a quantity of a new drug for human or veterinary use to a practitioner named in the letter of authorization for use in the emergency treatment of a patient under the care of that practitioner, if

(a) the practitioner has supplied to the Director information concerning

10-11-66 (i) the medical emergency for which the drug is required,

(ii) the data in the possession of the practitioner with respect to the use, safety and efficacy of that drug,

(iii) the names of all institutions in which the drug is to be used, and

(iv) such other data as the Director may require; and

(b) the practitioner has agreed to

(i) report to the manufacturer of the new drug and to the Director on the results of the use of the drug in the medical emergency, including information respecting any adverse reactions encountered, and

(ii) account to the Director on request for all quantities of the drug received by him.

10-11-66

(2) The Director shall, in any letter of authorization issued pursuant to subsection (1) state

(a) the name of the practitioner to whom the new drug may be sold;

(b) the medical emergency in respect of which the new drug may be sold; and

(c) the quantity of the new drug that may be sold to that practitioner for that emergency.

C.08.011. (1) Notwithstanding section C.08.002, a manufacturer may sell to a practitioner named in a lette of authorization issued pursuant to section C.08.010, a quantity of the new drug named in that letter that does not exceed the quantity specified in the letter.

10-11-66

(2) A sale of a new drug made in accordance with subsection (1) is exempt from the provisions of the Act and these Regulations.

Sale of Medicated Feeds

C.08.012. (1) Notwithstanding anything in this Division, a person may sell, pursuant to a written prescription of a veterinary practitioner, a medicated feed if

(a) as regards the drug or drugs used as the medicating ingredient of the medicated feed,

20-2-92 (i) the Director has assigned a drug identification number pursuant to section C.01.014.2, or

(ii) the sale is permitted by section C.08.005, C.08.011 or C.08.013;

(b) the medicated feed is for the treatment of animals under the direct care of the veterinary practitioner who signed the prescription;

(c) the medicated feed is for therapeutic purposes only; and

(d) the written prescription contains the following information:

(i) the name and address of the person named on the prescription as the person for whom the medicated feed is to be mixed,

12-9-80 (ii) the species, production type and age or weight of the animals to be treated with the medicated feed,

(iii) the type and amount of medicated feed to be mixed,

20-4-93 (iv) the proper name, or the common name if there is no proper name, of the drug or each of the drugs as the case may be, to be used as medicating ingredients in the preparation of the medicated feed, and the dosage levels of those medicating ingredients,

(v) any special mixing instructions, and

(vi) labelling instructions including

(A) feeding instructions,

(B) a warning statement respecting the withdrawal period to be observed following the use of the medicated feed, and

(C) where applicable, cautions with respect to animal health or to the handling or storage of the medicated feed.

(2) For the purpose of this section, "medicated feed" has the same meaning as in the Feeds Regulations.

EXPERIMENTAL STUDIES

Conditions of Sale

C.08.013. (1) Notwithstanding anything in this Division, a person may sell a new drug proposed for use in animals to an experimental studies investigator in a quantity specified by the Director for the purpose of conducting an experimental study in animals if

23-4-81 (a) the experimental studies investigator has been issued an experimental studies certificate pursuant to subsection C.08.015(1) and the certificate has not been suspended or cancelled pursuant to section C.08.018; and

(b) the drug is labelled in accordance with subsection C.08.016(1).

(2) For the purposes of this section and sections C.08.014 to C.08.018,

"experimental studies certificate" means a certificate issued pursuant to subsection C.08.015(1);

"experimental studies investigator" means a person named as the investigator in an experimental studies certificate;

"experimental study" means a limited test of a new drug in animals carried out by an experimental studies investigator.

Experimental Studies Certificate

C.08.014. (1) For the purpose of obtaining an experimental studies certificate, an applicant shall submit to the Director, in writing, the following information and material:

20-4-93
(a) the brand name of the new drug or the identifying name or code proposed for the new drug;
(b) the objectives and an outline of the proposed experimental study of the new drug;
(c) the species, number and production type of animals in respect of which the new drug is to be administered;
(d) the name and address of the manufacturer of the new drug;
(e) the address of the premises in which the experimental study is to be conducted;
(f) a description of the facilities to be used to conduct the experimental study;
(g) the name, address and qualifications of the proposed experimental studies investigator;
(h) the chemical structure, if known, and the relevant compositional characteristics of the new drug;
(i) the proposed quantity of the new drug to be used for the experimental study;
(j) the results of any toxicological or pharmacological studies that may have been conducted with the new drug;
(k) the written agreement referred to in subsection (2); and
(l) such other information and material as the Director may require.

(2) Where a food-producing animal is involved in an experimental study, the applicant referred to in subsection (1) shall, for the purposes of obtaining an experimental studies certificate, obtain from the owner of the animals, or from a person authorized by the owner, a written agreement not to sell the animal or any products from it without prior authorization from the experimental studies investigator.

(3) The Director may request the manufacturer of a new drug to submit to him samples of the new drug or of any ingredient of the drug and, in satisfactory form and manner, any other information that the Director requests and where such samples or information are not submitted, the Director may refuse to issu an experimental studies certificate.

C.08.015. (1) Where, on receipt of the information and material submitted pursuant to section C.08.014, the Director is satisfied that

23-4-81
(a) the applicant is qualified as an experimental studies investigator for the purposes of the proposed experimental study,
(b) the facilities for the conduct of the experimental study are adequate for the purposes of the proposed experimental study, and
(c) the proposed experimental study can be conducted without undue foreseeable risk to humans or animals,

the Director shall issue an experimental studies certificate for the purposes of the proposed experimental study and shall specify therein the quantity of the new drug that may be sold to the experimental studies investigator.

(2) Where, on receipt of the information and material submitted pursuant to section C.08.014, the Director is not satisfied that the requirements of paragraphs (1)(a), (b) and (c) have been met, he shall refuse to issue an experimental studies certificate.

Labelling

C.08.016. (1) The label of new drug that is sold pursuant to section C.08.013 shall show

20-4-93
(a) the brand name of the new drug or the identifying name or code proposed for the new drug;
(b) a warning statement to the effect that the drug is for use only in an experimental study in animals;
(c) the lot number of the drug;
(d) the name and address of the manufacturer of the drug; and
(e) the name of the person to whom the drug has been supplied.

21-7-88
(2) Sections C.01.004, C.01.005 and C.01.014 do not apply to a drug that is sold pursuant to section C.08.013 and labelled in accordance with subsection (1).

Conditions of Experimental Study

C.08.017. An experimental studies investigator shall

(a) use the new drug only in accordance with the outline of the experimental study;
7-6-01
(b) report immediately to the Director all serious adverse drug reactions associated with the use of the new drug;
(c) report promptly to the Director, on request, the results of the experimental study;

(d) return to the manufacturer, on request, all quantities of the new drug not used in the experimental study;
(e) maintain all records of the experimental study for a period of at least two years after the conclusion of the study and, on request, make such records available to the Director;
(f) report promptly to the Director any known disposition of animals involved in the study or of any products from the animals that is contrary to the terms of the agreement referred to in subsection C.08.014(2); and
(g) account to the Director, on request, for all quantities of the new drug received by him.

Suspension or Cancellation of Experimental Studies Certificate

C.08.018. (1) Where the Director is of the opinion that it is necessary in order to safeguard animal health or public health or to promote public safety, he may suspend for a definite or indefinite period or cancel an experimental studies certificate.

23-4-81

(2) Without limiting the generality of subsection (1), the Director may suspend or cancel an experimental studies certificate if

(a) the information and material submitted pursuant to section C.08.014 contains an untrue statement or contains any omission concerning the properties of the drug that were known or ought reasonably to have been known to the manufacturer or the experimental studies investigator;
(b) the labelling of the new drug is, at any time, false, misleading, deceptive or incomplete;
(c) the qualifications of the experimental studies investigator prove to be inadequate;
(d) there is evidence that the experimental studies investigator has not complied with the conditions referre to in section C.08.017; or
(e) an action of the manufacturer in respect of the new drug has resulted in his conviction for a violation of section C.08.002.

Non-prescription Drugs

C.09.001. This Division does not apply to

(a) a drug that is required by these Regulations or the Narcotic Control Regulations to be sold only on prescription, or
(b) a drug for use exclusively in animals.

Analgesics

General

C.09.010. No manufacturer or importer shall, after June 30, 1986, sell a drug for analgesia that contains a combination of

(a) a salt or derivative of salicylic acid with another salt or derivative of salicylic acid or with salicylamide; or
(b) acetaminophen with a salt or derivative of salicylic acid or with salicylamide.

29-5-86 **C.09.011.** Each label of a drug that is intended for internal use and contains acetaminophen, salicylic acid o a salt or derivative thereof shall, after June 30, 1986, carry a caution

(a) to consult a physician if the underlying condition requires continued use for more than five days; and
(b) that it is hazardous to exceed the maximum recommended dose unless advised by a physician.

2-2-84 **C.09.012.** Each label of a drug that is intended for internal use and contains salicylic acid or a salt or derivative thereof shall after June 30, 1986, carry a warning statement to consult a physician before taking the drug during the last three months of pregnancy or when nursing.

Acetaminophen

C.09.020. (1) The adult standard dosage unit of acetaminophen shall be 325 mg.

28-8-90 (2) The children's standard dosage units of acetaminophen shall be 80 mg or 160 mg.

C.09.021. (1) In this Division, "acetaminophen product" means a drug that contains

(a) acetaminophen as a single medicinal ingredient; or
(b) acetaminophen in combination with caffeine.

28-8-90 (2) No manufacturer or importer shall sell an acetaminophen product unless it meets the requirements of this Division.

(3) Revoked by P.C. 1990-1818 of August 28, 1990.

4-11-99 **C.09.022.** (1) Subject to subsections (2) to (4), an acetaminophen product sold in the form of a tablet, capsule or other solid dosage form intended for oral administration shall contain one adult standard dosage unit of acetaminophen per individual dosage form.

26-9-85 (2) An acetaminophen product in the form of a tablet, capsule or other solid dosage form intende for oral administration may contain 500 mg of acetaminophen per individual dosage form if it has a label that states that it is not a standard dosage unit product.

4-11-99 (3) An acetaminophen product sold in the form of a tablet, capsule or other solid dosage form tha is intended for oral administration may contain 325 mg of acetaminophen for immediate release and another 325 mg for subsequent release, if it has a label that states that it is not a standard dosage unit product.

(4) An acetaminophen product sold in the form of a tablet, capsule or other solid dosage form tha is intended for oral administration and that is specially recommended for children shall contain one children's standard dosage unit of acetaminophen per individual dosage form.

(5) An acetaminophen product in the form of a liquid that is intended to be taken as drops and that is specially recommended for children shall contain one children's standard dosage unit of acetaminophen per millilitre of the product.

4-11-99 (6) A package of an acetaminophen product described in subsection (5) shall be accompanied by a measuring device capable of accurately delivering 0.5 mL of the product.

(7) An acetaminophen product in the form of a liquid that is not intended to be taken as drops and that is specially recommended for children shall contain one children's standard dosage unit per teaspoon of the product.

(8) An acetaminophen product in the form of a liquid shall contain one adult standard dosage unit of acetaminophen per teaspoon of the product.

Salicylates

C.09.030. (1) The adult standard dosage unit of a salicylate shall be

(a) in the case of acetylsalicylic acid, sodium salicylate and magnesium salicylate, 325 mg; and
(b) in the case of choline salicylate, 435 mg.

(2) The children's standard dosage unit of a salicylate shall be

(a) in the case of acetylsalicylic acid, sodium salicylate and magnesium salicylate, 80 mg; and
(b) in the case of choline salicylate, 110 mg.

C.09.031. (1) In this Division, "salicylate product" means a drug that contains

(a) a salt or derivative of salicylic acid as a single medicinal ingredient;
(b) a salt or derivative of salicylic acid in combination with caffeine;
(c) a salt or derivative of salicylic acid in combination with one or more buffering agents or antacids; or
2-2-84 (d) a salt or derivative of salicylic acid in combination with caffeine and one or more buffering agents or antacids.

(2) No manufacturer or importer shall sell a salicylate product after June 30, 1986 unless it meets the requirements of this Division.

26-9-85 (3) No manufacturer or importer shall, until June 30, 1986, sell a salicylate product in a dosage unit other than one mentioned in this Division, unless the salicylate product was legally available for sale in Canada on February 1, 1984.

26-9-85 **C.09.032.** (1) Subject to subsections (2) and (3) and section C.09.035, a salicylate product in the form of a tablet, capsule or other solid dosage form intended for oral administration shall contain one adult standard dosage unit of a salicylate per individual dosage form.

(2) A salicylate product in the form of a tablet, capsule or other solid dosage form intended for oral administration may contain

(a) 500 mg of acetylsalicylic acid, sodium salicylate or magnesium salicylate, or
(b) 670 mg of choline salicylate

per individual dosage form if it has a label that states that it is not a standard dosage unit product.

(3) A salicylate product in the form of a tablet, capsule or other solid dosage form intended for oral administration may contain

(a) two adult standard dosage units of a salicylate per individual dosage form if the label of the salicylate product states that each individual dosage form contains two adult standard dosage units; and
(b) three adult standard dosage units of a salicylate per individual dosage form if the label of the salicylate product states that each individual dosage form contains three adult standard dosage units.

C.09.033. (1) Subject to subsection (2), a salicylate product in the form of a liquid shall contain one adult standard dosage unit of a salicylate per teaspoon.

(2) A salicylate product in the form of a liquid may contain

(a) two adult standard dosage units of a salicylate per teaspoon if the label of the salicylate product states that each teaspoon of the product contains two adult standard dosage units; and
(b) three adult standard dosage units of a salicylate per teaspoon if the label of the salicylate product states that each teaspoon of the product contains three adult standard dosage units.

2-2-84 **C.09.034.** A salicylate product that is claimed to be buffered shall provide at least 1.9 milliequivalents of acid neutralizing capacity per adult standard dosage unit of a salicylate.

C.09.035. A salicylate product in the form of a tablet, capsule or other solid dosage form intended for oral administration and that is specially recommended for children shall contain one children's standard dosage unit of a salicylate per individual dosage form.

DIVISION 10

Repealed by P.C. 1998-1461 of August 26, 1998.

SCHEDULE

Repealed by P.C. 1998-1461 of August 26, 1998.

TABLE

Repealed by P.C. 1998-1461 of August 26, 1998.